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CONTRIBUTORS

ABBOTT, MAUDE E., B.A., M.D., L.R.C.P. AND S. (EDIN.)

BABCOCK, ROBERT HALL, M.D.

BIRKETT, H. S., C.B., M.D., C.M., LL.D. (MCGILL)

BLUMER, GEORGE, M.D., M.A.

CHRISTIAN, HENRY A., M.D., LL.D.

GIBSON, ALEXANDER G., M.D., F.R.C.P.

HARE, H. A., M.D., LL.D.

HERRICK, JAMES B., M.D.

HOOVER, CHARLES F., M.D.

HOWARD, CAMPBELL P., M.D.

LANDIS, H. R. M., M.D.

LEWIS, SIR THOMAS, C.B.E., M.D., F.R.C.P., F.R.S.

LORD, FREDERICK T., M.D.

McMILLAN, THOMAS M., M.D.

McPHEDRAN, ALEXANDER, M.D., LL.D.

NORRIS, GEORGE WILLIAM, B.A., M.D.

OSLER, SIR WILLIAM, BART., M.D., F.R.S.

PACKARD, FRANCIS R., M.D.

RACKEMANN, FRANCIS M., M.D.

WARTHIN, ALDRED SCOTT, PH.D., M.D.

MODERN MEDICINE

ITS THEORY AND PRACTICE

IN ORIGINAL CONTRIBUTIONS BY AMERICAN AND
FOREIGN AUTHORS

EDITED BY

SIR WILLIAM OSLER, BART., M.D., F.R.S.

LATE REGIUS PROFESSOR OF MEDICINE IN OXFORD UNIVERSITY, ENGLAND; HONORARY PROFESSOR OF MEDICINE IN
THE JOHNS HOPKINS UNIVERSITY, BALTIMORE; FORMERLY PROFESSOR OF CLINICAL MEDICINE IN
THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA. AND OF THE INSTITUTE OF MEDICINE
IN MCGILL UNIVERSITY, MONTREAL, CANADA

THIRD EDITION, THOROUGHLY REVISED

RE-EDITED BY

THOMAS McCRAE, M.D.

PROFESSOR OF MEDICINE IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA, FELLOW OF THE ROYAL COLLEGE OF
PHYSICIANS, LONDON; FORMERLY ASSOCIATE PROFESSOR OF MEDICINE, THE JOHNS HOPKINS UNIVERSITY

ASSISTED BY

ELMER H. FUNK, M.D.

ASSISTANT PROFESSOR OF MEDICINE, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA

VOLUME IV

DISEASES OF THE RESPIRATORY SYSTEM—DISEASES OF
THE CIRCULATORY SYSTEM

ILLUSTRATED



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CONTRIBUTORS TO VOLUME IV

- MAUDE E. ABBOTT, B.A., M.D., L.R.C.P. AND S. (EDIN.),**
Assistant Professor of Medical Research and Curator of the Medical Museum,
McGill University, Montreal, Canada.
- ROBERT HALL BABCOCK, M.D.,**
Former Professor of Clinical Medicine and Diseases of the Chest in the College
of Physicians and Surgeons, Medical Department of the University of Illinois,
Chicago, Ill.; Associate on Staff of St. Luke's Hospital and Consulting Physi-
cian to the Pasavant Hospital, Chicago, Ill.; Director of the American Tuber-
culosis Association and of the Chicago Tuberculosis Institute, Chicago, Ill.
- H. S. BIRKETT, C.B., M.D., C.M., LL.D. (McGILL),**
Professor of Laryngology and Otology in McGill University; Laryngologist and
Otolgist to the Royal Victoria Hospital, Montreal, Canada.
- GEORGE BLUMER, M.D., M.A.,**
David P. Smith Clinical Professor of Medicine in the Yale Medical School, New
Haven, Conn.
- HENRY A. CHRISTIAN, M.D., LL.D.,**
Hersey Professor of the Theory and Practice of Physic in Harvard University;
Physician-in-Chief to the Peter Bent Brigham Hospital, Boston, Mass.
- ALEXANDER G. GIBSON, M.D., F.R.C.P.,**
Physician to the Radcliffe Infirmary, Oxford, England; Lecturer in Morbid
Anatomy in the University of Oxford, Oxford, England.
- H. A. HARE, M.D., LL.D.,**
Professor of Therapeutics, Materia Medica, and Diagnosis in Jefferson Medical
College; Physician to the Jefferson Hospital, Philadelphia.
- JAMES B. HERRICK, M.D.,**
Clinical Professor and Chairman of the Department of Medicine in Rush Medical
College of the University of Chicago; Consulting Physician to the Presbyterian
Hospital, Chicago, Ill.
- CHARLES F. HOOVER, M.D.,**
Professor of Medicine in the Medical College of Western Reserve University;
Physician to Lakeside Hospital, Cleveland, Ohio.
- CAMPBELL P. HOWARD, M.D.,**
Professor of Medicine in McGill University, Montreal, Canada; Physician to
the Montreal General Hospital; Formerly Professor of the Theory and Practice
of Medicine at the State University of Iowa.
- H. R. M. LANDIS, M.D.,**
Director of the Clinical and Sociological Departments of the Henry Phipps Insti-
tute, University of Pennsylvania, Philadelphia; Visiting Physician to the White
Haven Sanatorium, White Haven, Pa.
- SIR THOMAS LEWIS, C.B.E., M.D., F.R.C.P., F.R.S.,**
Physician and Lecturer in the University College Hospital, London, England;
Physician to Staff of the Medical Research Council; Honorary Consulting
Physician to the Ministry of Pensions, London, England.

FREDERICK T. LORD, M.D.,

Instructor in Clinical Medicine in the Medical School of Harvard University,
Boston, Mass.; Visiting Physician to the Massachusetts General Hospital,
Boston, Mass.

McMILLAN, THOMAS M., M.D.,

Assistant Physician to the Pennsylvania Hospital, Philadelphia; Cardiologist to
the Philadelphia General Hospital; Assistant Professor of Cardiology in the
Graduate School of Medicine of the University of Pennsylvania, Philadelphia.

ALEXANDER McPHEDRAN, M.D., LL.D.,

Professor Emeritus of Medicine in the University of Toronto, Toronto, Canada;
Consulting Physician to the Toronto General Hospital and the Hospital for
Sick Children, Toronto, Canada.

GEORGE WILLIAM NORRIS, B.A., M.D.,

Professor of Clinical Medicine in University of Pennsylvania; Physician-in-Chief
of Medical Service "A" at the Pennsylvania Hospital, Philadelphia.

SIR WILLIAM OSLER, BART., M.D., F.R.S.,

Late Regius Professor of Medicine in Oxford University, Oxford, England.

FRANCIS R. PACKARD, M.D.,

Surgeon to Out-Patient Department for Diseases of the Nose, Throat, and Ear,
of the Pennsylvania Hospital, Philadelphia.

FRANCIS M. RACKEMANN, M.D.,

Physician to Out-Patients at the Massachusetts General Hospital, Boston, Mass.;
Instructor in Medicine in Harvard Medical School, Boston, Mass.

ALDRED SCOTT WARTHIN, PH.D., M.D.,

Professor of Pathology and Director of the Pathological Laboratories in the
University of Michigan, Department of Medicine, Ann Arbor, Mich.

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PART I

DISEASES OF THE RESPIRATORY TRACT

CHAPTER I

THE PHYSIOLOGY OF RESPIRATION

By GEORGE W. NORRIS, M.D.

AND

THOMAS M. McMILLAN, M.D.

RESPIRATION in its broadest sense includes all those processes by which the oxygen of the external air is taken into the blood and transported to the tissues, and the carbon dioxide given off by the tissues is expelled from the body. Those portions of this complex mechanism that are concerned with the gaseous transportation and interchange between tissues and blood are spoken of as Internal Respiration; while those having to do with the gaseous interchange between the blood and the external air are referred to as External Respiration. For both external and internal respiration the continuous removal of used air and the constant renewal of fresh air in the lungs are essential.

RESPIRATORY MOVEMENTS

The constant renewal of fresh air and expulsion of the used air are accomplished by the movements of inspiration and expiration which succeed each other normally with but slight pause between the two acts. These movements of respiration vary normally under a variety of conditions. Among these varying factors may be mentioned age, psychic disturbances and volition. In addition to these more or less normal factors there are various diseased states that greatly alter the normal respiratory movements.

Inspiration is accomplished by the enlargement in all diameters of the thoracic cage. The elastic lung tissue follows this enlarging movement and air is thus sucked into the vital portions of the lungs. The diminution of the capacity of the thorax allows the elastic lungs to contract and force out the inspired air. This constitutes expiration. Under all ordinary conditions, expiration is a passive process and does not involve the active contraction of any of the respiratory muscles.

FIG. 1

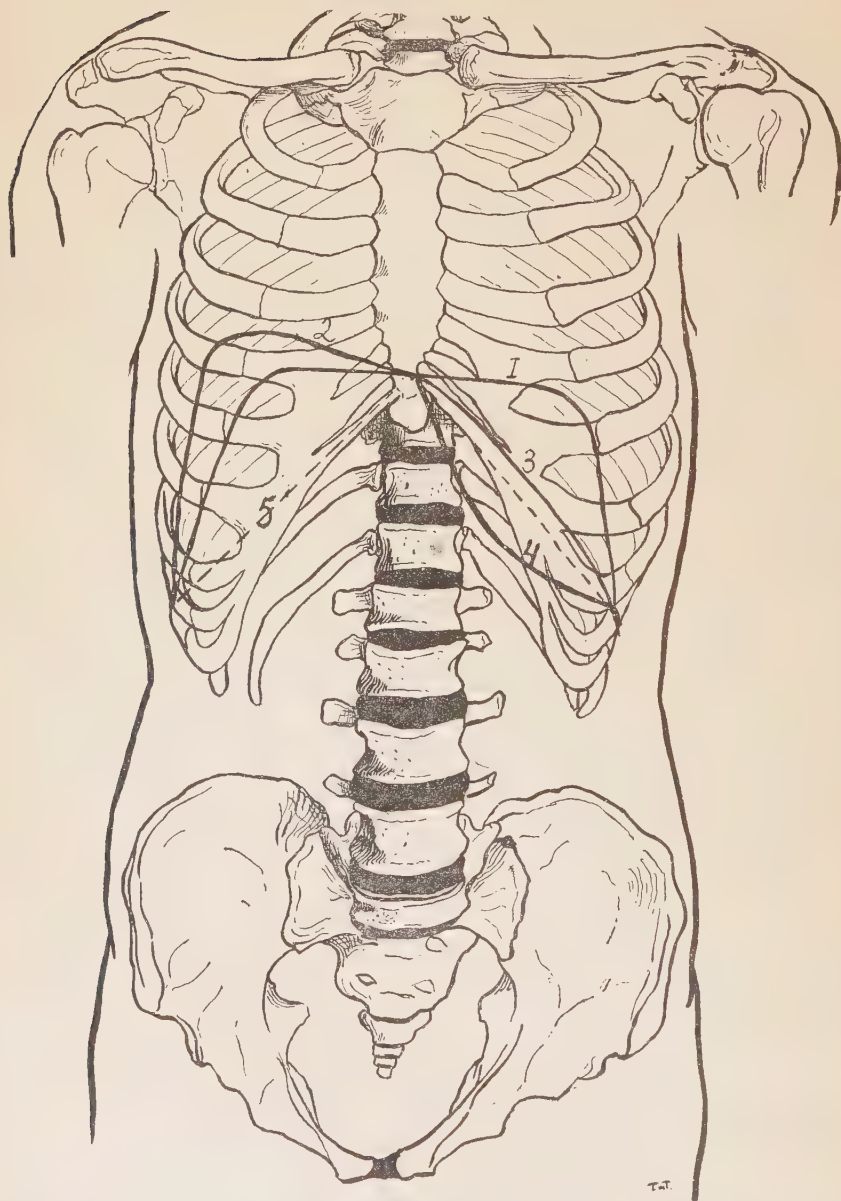


Diagram to show the effect of position of the diaphragm on the movement of the rib margins. Line 1. Normal position of the diaphragm. Rib margins move outward during inspiration. Line 2. High position of the diaphragm. Outward movement of the rib margins accentuated. Line 3. Low position of the diaphragm. Costal margins move inward during inspiration. Line 4. Very low position of the diaphragm. The line of traction from the central tendon to the rib margins is disadvantageous. The costal margins move outward during inspiration. Line 5. The line of traction of the diaphragm. (From R. G. Pearce.)

FIG. 2

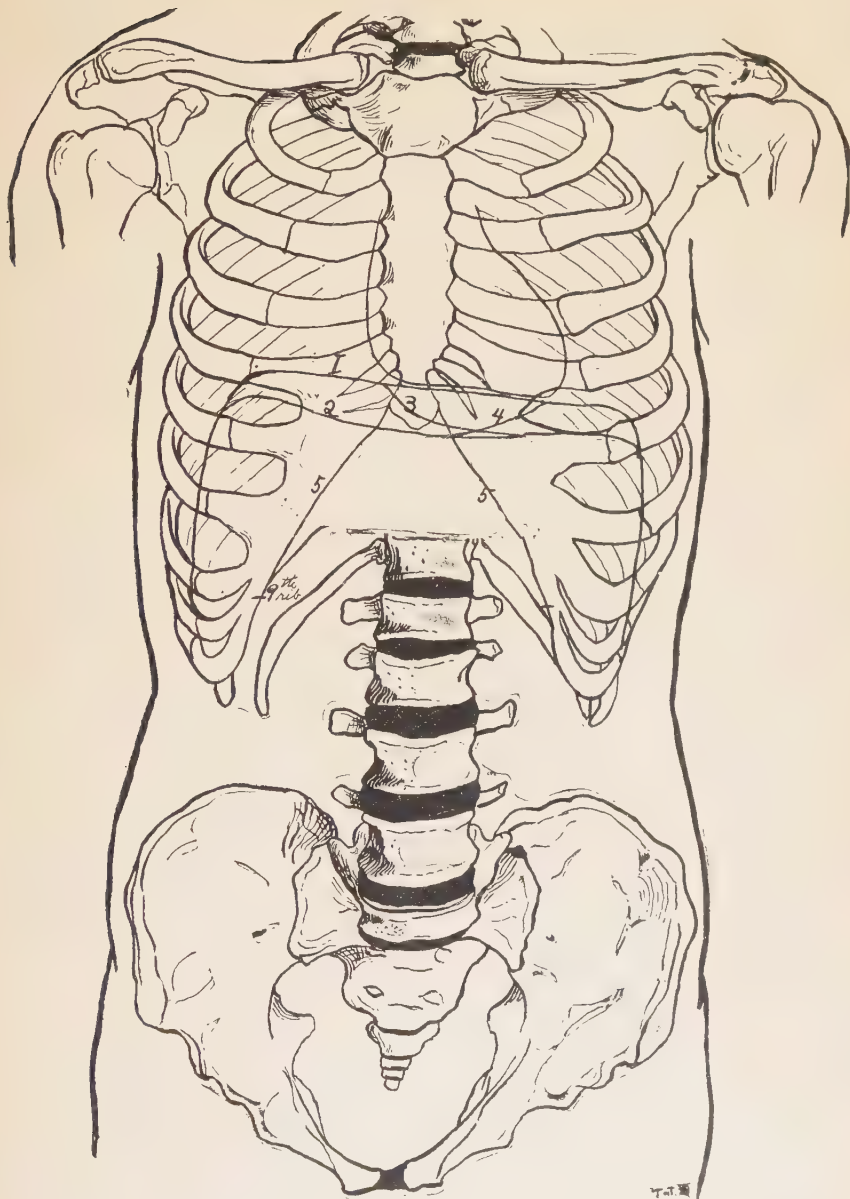


Diagram to show the effect of clinical displacements of the diaphragm on the movements of the rib margins. Line 1. Normal position of the diaphragm. Costal margins move outward during inspiration. Line 2. Position of the diaphragm in general cardiac enlargement. Costal margins move toward median line. Line 3. Position of the diaphragm in left-sided cardiac enlargement. Left costal margin is fixed or moves inward, while right costal margin moves outward during inspiration. Line 4. Position of diaphragm in right-sided cardiac enlargement. Right costal margin is fixed or moves inward during inspiration, while the left moves outward normally. Line 5. Costal margins. (From R. G. Pearce.)

Intrapleural Pressure.—There is a slight but definite negative pressure in that space between the lungs and the thoracic wall which is designated the Intrapleural Space. If this is measured at the end of expiration it is found to be around -5 mm. Hg. At the end of inspiration the negative pressure is found to be increased to -10 mm. Hg. This increase in the negative pressure on inspiration is the factor responsible for the expansion of the lungs and for the accompanying inrush of air at each inspiration. As the negative pressure increases there is an increased pull on the elastic lungs which causes these to expand and follow the enlargement of the thoracic cage. The negative pressure in the pleural space exists because this space has no access to outside gases and because the lungs are elastic and tend to recoil, and thus exert a pull on this already airless space.

The Muscular Mechanism of the Respiratory Movements.—The acts of enlarging and diminishing the thoracic capacity are accomplished by a complex muscular mechanism. Quiet inspiration is accomplished principally by the diaphragm and the intercostal muscles. When the respiration becomes more labored for any reason a number of other muscles, the accessory muscles of respiration, come into play.

The Diaphragm and Intercostal Muscles.—The diaphragm has for its part the increase of the longitudinal diameter of the thorax. The antero-posterior and transverse diameters are increased almost solely by the intercostal muscles. (Extension of the spinal column aids in enlarging the thorax in a slight degree.) Hoover in studies on the respiratory mechanism has pointed out several signs of considerable clinical value which have to do with the movements of the upper four ribs and the costal margins. The second, third and fourth ribs normally show an undulatory movement as inspiration progresses, of such a nature that the ribs begin their upward outward movement in order from above downward, while each successive rib moves further than the rib immediately above it. When the rib movement does not take place in this orderly fashion, it is an indication of diminished ventilation of the underlying lung. This indicates a decreased extensibility of the lung tissue. Hoover has pointed out that decreased extensibility is a change that occurs earlier in disease than any other change in lung tissue and hence is an indication of early pathological change in the lungs.

Another sign that Hoover pointed out has to do with the movement of the costal margins. The effect of the contraction of the intercostal muscles would result in the upward outward movement of the costal margins. Isolated contraction of the diaphragm would result in pulling the distal points of its attachment, the rib margins, inward. The more arched the diaphragm, the less advantageous would its line of traction be, and consequently the less would be the inward pull on the rib margins. Conversely, the flatter the arch of the diaphragm, the more effective its line of traction and the greater the inward pull on the costal margins. Under normal conditions, the line of traction from the central tendon to the rib margins is such that the inward pull of the diaphragm on the rib margins is overcome by the antagonistic intercostal muscles and the rib margins move outward. Hoover has emphasized that if the diaphragm is flatter than it should be because of pleural effusion, pericardial effusion,

cardiac enlargement, or any other cause, its line of traction would be straighter, the intercostals would be overcome, and the rib edges would move inward. If both sides of the arch were flattened, both costal borders would move inward on inspiration. If one costal border moved outward normally, while the other moved inward, some cause of flattening of the arch on the side that moved inward could be looked for. (See Figs. 1 and 2.)

Pulmonary Ventilation.—During quiet respiration, about 500 cc. of air enter and leave the lungs. This is spoken of as the tidal air. By forcible inspiration perhaps 1500 cc. more can be made to enter the lungs. This is known as complementary air. A forcible expiratory effort after the completion of a normal expiration will expel possibly 1500 cc.—the supplemental air. These three amounts together make up the *vital capacity*. To express this in another way, the vital capacity is the amount of air that can be forcibly expired after a forced inspiration. In recent years this subject has acquired a considerable clinical importance.

The work of Peabody and Wentworth¹ showed that the dyspnoea of heart disease depends on an inability to breathe deeply, and that this limitation corresponds directly with the vital capacity. It is obvious that inability to breathe deeply may depend on many factors beside heart disease. Thoracic tumors, infarcts, pleural effusions, etc., might cause it simply by diminishing the available space for lung expansion. Likewise changes in the lung tissues which cause a diminution in the expansibility of the lungs—fibrosis, for example—might limit the normal depth of respiration. The reason for the lowered vital capacity in heart disease is not altogether clear. It usually is seen in those forms of heart disease in which the lungs are affected by congestion and exudation into the alveoli. There must be normal standards with which comparisons can be made and the vital capacity varies considerably in health. The normal standards based on surface area are probably the most accurate, though Hewlett and Jackson² found that standards based on height alone were but slightly less accurate. They pointed out that the latter standards have the advantage of not being effected by oedema.

As a method of detecting heart disease, vital capacity can be no more than a partial guide; for many conditions other than heart disease cause a lowering of this value. Furthermore some normal persons have a vital capacity that shows a greater percentage departure from the normal than the accepted 15 per cent. As a means of gauging the clinical progress of a patient with heart disease the method is extremely important and valuable; the vital capacity increases as the circulatory phenomena improve and decreases as they deteriorate. Attempts have been made to extend the clinical value of this finding to diseases other than heart disease. Its value in other diseases has not been sufficiently demonstrated to make the method of clinical importance.

Alveolar and Dead Space Air.—In addition to the portions of the air in the lungs that go to make up the vital capacity, there is another division of the lung air that is of some importance. The air in the lungs may be

¹ *Arch. Int. Med.*, 1917, **20**, 443.

² *Ibid.*, 1922, **29**, 515.

divided into the alveolar air and the dead space air. The alveolar air is that which is in contact with the alveolar epithelium. The dead space air is that which fills the other portions of the lungs. The dead space cannot be defined anatomically; rather is it a purely functional space. However the air it contains plays a very important physiological role; it acts as a mechanical buffer in preventing too sudden changes in the chemical composition of the alveolar air, which is so important in regulating the chemical composition of the blood, and, through this, the respiratory centre.

THE REGULATION OF THE RESPIRATORY MOVEMENTS

The Respiratory Centre.—Each act of respiration involves the activity of many groups of muscles and these muscles must act coördinately; this requires the coincident discharge of nervous impulses from many centres. The coördination of this complex nervous action is brought about by a chief respiratory centre in the medulla which regulates the discharge of impulses from all the subsidiary nerve centres. The respiratory centre is bilateral. The two sides are connected with each other, and the centre of each side is connected with the subsidiary nerve centres of both sides. This structure, poorly defined anatomically, governs the discharge of all impulses from the various nerve centres that directly control the respiratory muscles. The factors that influence the respiratory centre are therefore the factors that control the respiratory movements.

The Control of the Respiratory Centre.—Two chief theories have been held as explaining the control of the respiratory centre. One theory held that its action depended wholly upon nervous influences from distant structures: that its action was controlled reflexly. The other theory assumed that its activity was dependent upon chemical and metabolic changes occurring in its environment which made its action an automatic one, much after the manner that the rhythmic beating of the heart is automatic. Recent research has shown that both factors, the chemical and the nervous, have an important part in regulating the constantly changing, well ordered activity of the respiratory centre.

Chemical Control of the Respiratory Centre.—That its control is chiefly automatic and not dependent on afferent nerve impulses has been shown by experiments that isolate the centre from all afferent stimuli. Under these conditions respiration continues. The activity of the respiratory centre is essentially controlled by the chemical composition of the blood. Nervous influences guide this control much as sensory impulses from joints and muscles aid in the muscular control of the extremities. The evidences of the sensitiveness of the respiratory centre to chemical changes in the blood are abundant. The effects of change in the reaction of the blood can be shown, in a rough way, by introducing acid or alkali directly into the circulation. If acid is introduced into the central end of a vein the respiration is greatly stimulated; if alkali is similarly used the respiration is depressed. In studying the control of respiration it soon became apparent that changes in the gaseous composition of the inspired air profoundly affected respiration.

Respiratory Effects of Changes in the Gaseous Composition of the Inspired Air.—Early studies on this problem were made by observing the effects of asphyxia. In this there is an early stage of hyperpnœa, during which respiration is greatly stimulated. Rosenthal believed this to be due to an insufficiency of oxygen. Traube believed the effective respiratory stimulus to be the excess of carbon dioxide that accumulated in the blood under the conditions of asphyxia. The greater element of truth lay in Traube's interpretation. More light was thrown on this question by later experiments in which a subject respired in an air-tight chamber. In such an experiment, as the carbon dioxide accumulates and the oxygen diminishes, the respirations are stimulated and hyperpnœa occurs. If such an experiment be repeated but with provisions for absorbing the carbon dioxide, no increase in the respirations occurs, at least not until the available oxygen is very greatly reduced. This experiment shows definitely that increase in the CO_2 content of the blood, and not a diminution of oxygen, is the early effective respiratory stimulus under conditions of asphyxia. When the available oxygen in the inspired air becomes greatly reduced, there is a stimulation of respiration. The role of lack of oxygen as a respiratory stimulus will be discussed later.

Relation Between the CO_2 Tension of Alveolar Air and the Blood.—The CO_2 content of venous blood is higher than that of the alveolar air. The CO_2 tension of the arterial blood leaving the lungs is the same as that of the alveolar air. Moreover the CO_2 tension of the arterial blood will follow the alveolar tension even when the latter is widely varied experimentally. The exchange of CO_2 between the blood and the alveolar air is controlled by physical laws of gas diffusion according to which gases diffuse from a point of higher pressure to a point of lower pressure until an equilibrium is established. Therefore the determination of the alveolar CO_2 tension gives an accurate measure of the tension of this gas in the arterial blood.

With this in mind, the role of the CO_2 tension of the blood in stimulating respiration can be shown even more clearly by experiments in which the tension of this gas in the air breathed is quantitatively increased. Haldane has shown that if the CO_2 in the air breathed is raised to 2 per cent., the depth of respiration is increased by 30 per cent., and the total pulmonary ventilation by 50 per cent. If the CO_2 is increased to 3 per cent., the total ventilation is increased by 126 per cent. If, during such an experiment, the alveolar CO_2 is determined, it is found to be normal in spite of its increased percentage in the inspired air. From this it must be concluded that the respiratory centre is exquisitely sensitive to even minute changes in the CO_2 tension of the blood, and responds by increasing the rate and depth of breathing. This increased respiration sweeps off the excess of CO_2 , and thus keeps the tension of this gas constant.

In brief it may be said that want of oxygen or anoxemia can stimulate respiration under certain abnormal conditions. The sensitiveness of the respiratory centre to the chemical changes that accompany even a minute increase in the CO_2 tension of the blood is the more important stimulating factor. Indeed this may be regarded as the only active chemical factor in controlling the respiratory movements under normal conditions.

We will next consider the way in which CO_2 effects these profound changes in the activity of the respiratory centre. This requires a consideration of the acid base equilibrium.

The Acid Base Equilibrium of the Blood.—The relation of the acids and bases of the blood is ordinarily so regulated that the hydrogen-ion content of the blood remains very constant. The alkali or base may change to some extent, but the chief variations occur in the acid content. The acid of the blood exists in three forms: fixed inorganic acid, of which phosphoric may be taken as the representative, fixed organic, represented by lactic acid, and volatile acid represented by CO_2 . The first two acid groups vary but slightly. The chief changes in the acidity are caused by changes in the CO_2 . Since this substance is excreted solely by the lungs, and since it acts as the chief stimulus of respiration, it is clear that there is a very close relationship between the acid base equilibrium of the blood and respiration. We have spoken so far only of the lungs as an agent for maintaining the acid base equilibrium. There are two other organs that play a part in maintaining this equilibrium. Their role is not so active or continuous as is that of the lungs. We will discuss subsequently the part that the liver and kidneys play in this regulation.

The Manner in which CO_2 Accomplishes Respiratory Stimulation.—In the preceding paragraph it was pointed out that CO_2 was the volatile acid constituent of the blood, and that a rise in the CO_2 tension of the blood brings about an increase in the hydrogen-ion content. Is the higher hydrogen-ion concentration, or the increased CO_2 *per se* the effective respiratory hormone?

This is not an easy question to answer experimentally. Any increase in the hydrogen-ion content of the blood, whether due to excessive amounts of CO_2 , organic acids or volatile acids, will profoundly stimulate the respiratory centre. There is some evidence that CO_2 *per se* may act as a respiratory stimulus. Haldane, for one, does not regard this evidence as conclusive or valid. It is probably correct to regard the increased hydrogen-ion content that accompanies increase in the CO_2 tension of the blood as the effective agent in controlling the activity of the respiratory centre.

The sequence of events in the usual instances of increased breathing is first, an increase in the CO_2 content of the blood and an accompanying increase in the hydrogen-ion content, and second, increased respiration which sweeps out the excess of CO_2 and restores the normal acid base equilibrium of the blood. However this sequence of events is not always seen. It must be borne in mind that marked hyperpnœa can occur with a low blood and alveolar CO_2 tension. This is seen notably in clinical states of acidosis. The cause of the hyperpnœa is an increased blood acidity caused not by the volatile CO_2 , but by organic acids. The increased respiration sweeps out the CO_2 and lowers its concentration in the blood and alveolar air. Therefore increased hydrogen-ion concentration of the blood is the chief stimulus of respiration.

We have so far only considered CO_2 and changes in the acidity of the blood as controlling factors of the respiration. Under certain abnormal conditions, a want of oxygen can act as a stimulus of respiration.

The Effects of Anoxemia Upon Respiration.—The respiratory phenomena that follow upon oxygen want are increased breathing, a lowering of the alveolar CO_2 (which continues for some time after the anoxemia is ended) and a high respiratory quotient. The increased breathing differs somewhat depending on whether the anoxemia is acutely induced or gradually brought on. If it comes on quickly there is an initial marked hyperpnœa that gradually subsides. If the anoxemia comes on more slowly, the sharp initial increase in the respirations is not noted.

According to Haldane and his co-workers want of oxygen stimulates respiration by rendering the respiratory centre more sensitive to the ordinary concentrations of CO_2 . When sudden lowering of the oxygen tension occurs, the centre being more sensitive to the existing CO_2 tension, there is an immediate increase in the breathing. This sweeps out CO_2 and thus lowers the level of this gas in the blood. When the lower level is reached the increased breathing subsides. This explains why the marked initial hyperpnœa is not seen when the oxygen tension is gradually reduced: there is time for a gradual establishment of a lower CO_2 level. According to this conception the respiratory centre is still controlled by the hydrogen-ion concentration of the blood, even during anoxemia; for even under these conditions, if the alveolar CO_2 be increased or decreased the breathing changes accordingly.

The control of respiration is therefore a very complex affair in which both the CO_2 tension and the oxygen tension are important factors. Previously we have indicated that the respirations were governed almost solely by the pressure of CO_2 . We must now modify this, for the effective amount and tension of CO_2 is a relative quantity which is governed by oxygen tension. With a high oxygen tension a relatively higher tension of CO_2 is required to effect the respiration; while with a low oxygen tension, a lower CO_2 tension is effective. This interrelation of CO_2 and oxygen in controlling respiration is shown by an important experiment of Henderson. If an animal is subjected to excessive artificial respiration until the CO_2 tension is greatly reduced, a prolonged apnœa follows its cessation and the animal may die without again attempting to breathe. The interpretation of this is that if the CO_2 tension is below a certain critical level, the profoundest anoxemia will not stimulate respiration.

The initial increased breathing in anoxemia washes out the CO_2 and establishes a lower tension of this gas. When this is accomplished, the stimulating effect of CO_2 on the respiration is removed and the breathing becomes quieter. This furthers the vicious circle for the alveolar oxygen tension then becomes lower. If the tension of CO_2 in the inspired air is increased, the depth and frequency of the respirations will be increased. This will increase the alveolar oxygen tension and thus in a measure compensate the anoxemia. This principle has been used in treating carbon monoxide poisoning. In this and in all other forms of anoxemia, the so-called *Bohr effect* is probably active in keeping up the anoxemia. Bohr found that in the presence of low CO_2 tension, the hemoglobin holds on more tightly to its oxygen. In anoxemia from any cause the CO_2 tension is lowered. The tissues therefore are deprived of oxygen not only because of the lowered tension of this gas in the blood, but also because the hemo-

globin gives up the oxygen it does carry less readily. It is probable that breathing CO_2 in carbon monoxide poisoning is beneficial not only because it increases the respirations, and thus the oxygen tension, but also because it overcomes the Bohr effect by increasing the CO_2 of the blood.

This theory of anoxemia assumes that want of oxygen *per se* stimulates the respiratory centre by rendering it more susceptible to stimulation by the existing CO_2 tension. This is by no means the only hypothesis brought forward to explain the respiratory phenomena of anoxemia. A widely accepted explanation of these phenomena is based on the so-called "lactic acid theory."

The Lactic Acid Theory.—One of the difficult facts to explain in anoxemia is the continuance of the low alveolar and blood CO_2 for a considerable time after the want of oxygen is relieved. To explain this, many have had recourse to the lactic acid theory. According to this, in the presence of insufficient oxygen, the processes of oxygenation do not proceed to completion but stop at an intermediary stage. The chief of these products of improper oxygenation is lactic acid. The explanation, as it is applied to anoxemia, is that sufficient of this acid is set free in the blood to increase the hydrogen-ion concentration, stimulate the respiratory centre, and bring about the increased respiration that is seen in anoxemia. As this is a non-volatile acid, it must be got rid of by the kidneys. The excretion of this acid by the kidneys in the form of lactate is a process that requires time and thus the long duration of the low alveolar CO_2 is explained.

This hypothesis is attractive by making it possible to explain increased breathing in all instances on the basis of an increase in the hydrogen-ion concentration of the blood. Much indirect evidence favors it but there is certain direct evidence against its being a responsible factor in causing the respiratory phenomena of anoxemia. The increased breathing of high altitudes is undoubtedly due to anoxemia but in studying specific examples under these conditions no increase in the urinary or blood lactic acid was found. Moreover the acid and ammonia of the urine was decreased, the urine becoming alkaline. These findings were hardly in accord with the theory that under conditions of anoxemia there was an acidosis. To understand these factors it is necessary to recall that the acid base equilibrium of the body is controlled by at least three factors. The lungs, by holding back or getting rid of CO_2 , furnish the most responsive and labile mechanism. The liver, by increasing or decreasing the amount of ammonia formed, also plays a role. The kidneys likewise have a part in the acid base control, for they respond to even minute changes in blood alkalinity by secreting more alkali or more acid. They also keep normal the proportion of Na., K, and other salts in the blood, and thus aid in keeping normal the dissociation curve of CO_2 .

Haldane and his associates, and Haggard and Henderson, independently and by different methods, arrived at the same conclusion: that in anoxemia there is not an acidosis but an alkalosis, and that the kidneys and liver respond in a normal manner to this alkalosis. The diminished ammonia and acid excretion and increased alkali output in the urine tend

to compensate the alkalosis but never quite do so; for the alveolar CO_2 remains low even after the want of oxygen is ended. Compensation by the liver and kidneys explains why the low CO_2 continues for some time after the anoxemia is ended. That there is an alkalosis and not an acidosis in anoxemia has an important clinical application. Haldane cites as an example having seen numerous patients with acute anoxemia following gassing being given alkali on the theory that the anoxemia had caused an acidosis. What had actually been caused was an alkalosis.

Summary.—Oxygen want causes an increase in the respiration. This results in the sweeping off of CO_2 with a resultant low alveolar CO_2 tension. This brings about an alkalosis. The kidneys and liver attempt to compensate this alkalosis by excreting less ammonia and acid, and by getting rid of the excessive alkali. This compensation, except in slight degrees of anoxemia, is incomplete as evidenced by the continued low CO_2 pressure.

The Causes of Anoxemia.—**Anoxemia Due to Defective Saturation of the Arterial Hemoglobin with Oxygen.**—Shallow breathing has been shown to be an important cause of this variety of anoxemia by Priestley, Haldane and Meakins. During shallow breathing, all portions of the lung do not expand uniformly and therefore the arterial blood leaving the lungs contains considerable under-oxygenated blood. This increment may be so large that the mixed blood from the various portions of the lungs may be seriously under-oxygenated. Haldane has pointed out the great clinical importance of shallow breathing. In any case it may cause unequal ventilation of the alveoli and thus bring on serious anoxemia.

Fatigue of the Respiratory Centre.—The commonest cause of shallow breathing is fatigue or failure of the respiratory centre. Again Haldane has stressed the importance of this and pointed out its bearing on anoxemia. Chronic fatigue of the respiratory centre is seen in the breathing of neurasthenic states and in other conditions. There is a condition of acute fatigue or failure in which rapid shallow breathing begins suddenly. It is associated with a sense of suffocation and often with anginal pains. This condition may be a cause of sudden, otherwise unexplained death.

Deficiency in the Partial Pressure of Oxygen in the Inspired Air.—This is the cause of the anoxemia of high altitudes and is discussed more fully elsewhere.

Insufficient Time for Sufficient Oxygen to Penetrate the Alveolar Epithelium.—This cause of anoxemia may be important, and is Haldane's explanation of the anoxemia following the inhalation of irritating gases. It is likewise regarded by some observers to be the cause of symptoms accompanying exercise in untrained persons.

Anoxemia Caused by Some Fault in the Carrying Power of the Blood for Oxygen.—This group includes CO poisoning and various types of methemoglobinemia, which are discussed elsewhere.

The Clinical Importance of Anoxemia.—We are in the main indebted to Haldane for showing the dangerous significance of even slight degrees of anoxemia if long continued. There are practically no reserves of oxygen in the body, and no tissue can endure a long oxygen deprivation and

remain undamaged. In many diseases death results not primarily from the disease but secondarily from anoxemia. Therefore the early recognition of even slight degrees of anoxemia is of great clinical importance.

The Recognition of Anoxemia Clinically.—The principal sign of anoxemia relied on by clinicians is the presence or absence of cyanosis. This sign is to a certain degree unreliable for there may be anoxemia without cyanosis. This results through the operation of the Bohr effect previously mentioned. The hemoglobin holds on to its oxygen very firmly when the CO_2 content of the blood is low. Therefore the tissues may be greatly in want of oxygen, yet, because of a low CO_2 content, the blood holds on more firmly to its oxygen and thus remains non-cyanotic. Perhaps one of the best clinical indications of slight anoxemia is rapid shallow breathing; for if anoxemia is not present it will soon be brought on by this type of breathing.

The Nervous Regulation of Respiration.—Though the chemical state of the blood is the important factor in regulating the depth and rhythm of respiration, nervous impulses have an important part in effecting respiration. Afferent stimuli from many peripheral areas greatly effect respiratory movements. The effects of psychic disturbances, of heat and cold and of pain, etc., are frequently observed, and are examples of nervous influence upon respiration. The nervous impulses that exercise a more or less constant influence over respiration are transmitted through the vagi. Cutting or stimulating these nerves alters the respiratory movements very definitely. At one time it was thought that the alternate expansion and retraction of the lungs stimulated the vagi and furnished the only stimulus for respiration. We know now that chemical effects are the chief controlling factors, and that nervous influences are much less important.

The important part that afferent vagal stimuli play in the control of respiration has recently been reinvestigated by Haldane and his associates. They showed that if the normal inspiratory or expiratory movement be suddenly interrupted, the respiratory centre is influenced by this interruption and responds by giving off a more powerful and prolonged discharge in an effort to overcome the interference. "The respiratory centre does not act independently of the lung movements; but inspiratory and expiratory discharges of the centre go hand in hand with actual inspiration and expiration as if the centre were one piece with the lungs" (Haldane). Experiments on cutting and freezing the vagi led Haldane to believe that the coördination of the discharges of the respiratory centre with the actual movements of the lungs is accomplished through afferent stimuli conveyed by the vagi.

According to Haldane, in normal breathing, inspiration is terminated when the distention of the lungs reaches a certain degree. This distention results in an inhibitory stimulus being transmitted up the vagi, which in turn results in the onset of expiration. Expiration then continues until a certain degree of deflation is accomplished, when again another stimulus is transmitted through the vagus which terminates this phase and again initiates the inspiratory phase.

This nervous mechanism, which is referred to generally as the *Hering-*

Breuer reflex, therefore plays an extremely important part in determining the depth of respiration, the points at which inspiration and expiration set in. "Where the chemical regulation of the respiratory centre exerts its preponderating influence is in determining the extent to which inflation and deflation of the lungs must extend in order that the Hering-Breuer reflex should be effective" (Haldane). The early demands for increased pulmonary ventilation are ordinarily met through the mechanism of this reflex; the points of the beginning of inspiration and expiration are set farther apart, causing an increase in the depth of respiration. As the demands become greater, they are met by an increase in the rate as well as the depth of the respiratory movements. If this important reflex becomes upset, inspiration and expiration become abnormally short. Then when increased demand occurs increased ventilation must be accomplished by an increased rate, rather than depth, of respiration. It is not unlikely that the breathlessness of many diseased conditions may ultimately be explained on the basis of disturbance of this reflex.

Summary.—There are two factors active in controlling respiration. One is the chemical state of the blood, of which the hydrogen-ion concentration is the most important element. Want of oxygen, while never a factor in controlling respiration under normal conditions, does profoundly effect respiration when it exists in extreme degrees. The other factor is a nervous one by which afferent stimuli along the vagi determine respectively the beginning of inspiration and of expiration.

Of these two factors the chemical one is the more important; for rhythmic respiration will continue even with the respiratory centre isolated from all afferent nervous influences. Under these circumstances, however the respirations are imperfect and not so readily responsive to sudden demands. *The chemical conditions determine the total pulmonary ventilation; the Hering-Breuer reflex plays a leading role in determining how this shall be accomplished.*

The Absorption, Transportation and Discharge of O and CO₂ by the Blood.—Having discussed the control and mechanism of the respiratory phases, several other features of respiration in its broadest sense remain to be considered. The ultimate purpose of respiration is to supply oxygen to the tissues where the vital metabolic processes occur, and to remove the CO₂ formed as a result of these processes. We must now consider the entrance of oxygen into the blood, its transportation and its discharge to the tissues, the transportation of CO₂ by the blood and its exchange from the blood to the alveolar air.

It is necessary to recall that there are certain laws governing the absorption of gases by liquid substances. The amount of gas that a liquid will take up depends among other things upon the pressure of the gas. If the pressure of the gas is doubled twice the amount is absorbed. There is a constant movement of the gas molecules from the point of higher pressure to the point of lower pressure, regardless of whether the high point is in the fluid or in the gaseous atmosphere surrounding it. The mechanism is such that an equilibrium is constantly being sought, so that the number of molecules of gas entering the fluid media exactly equals the number of molecules of gas leaving the liquid. There are other less important fac-

tors that influence gas absorption by liquids. Among these temperature and the solid content of the fluid solvent may be mentioned.

The Transportation of Oxygen by the Blood.—According to the laws of gas absorption, the amounts of gases in the blood will depend to a large extent upon the pressures of the gases that exist in the alveolar air. In spite of the frequent respiratory acts, the composition of the alveolar air changes but slightly under ordinary conditions. This comes about because the tidal air is constantly being diluted by the much larger quantity of dead space air, the latter acting as a sort of buffer in preventing too rapid changes in the gaseous proportions of the alveolar air.

When the actual amount of oxygen in the arterial blood is studied, it is found that this amount is at least forty times more than the blood could absorb at the partial pressure of the oxygen in the alveolar air, were the process one of mere physical solution. It is clear that there must be some substance in the blood with a high chemical attraction for oxygen with which this gas unites in a chemical combination. This substance is hemoglobin. The union of oxygen with hemoglobin is very unstable but being a true chemical reaction, it obeys certain chemical laws, and is therefore a reversible reaction after the formula $\text{Hb} + \text{O}_2 \rightleftharpoons \text{HbO}_2$.

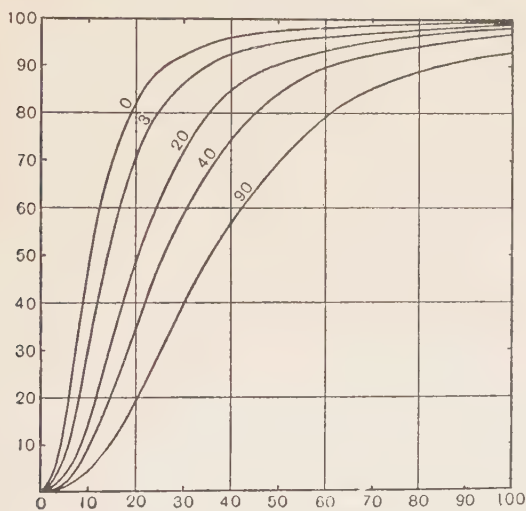
In human blood the partial pressure of oxygen varies widely. At the alveolar end of the arterial system this gas has a partial pressure of approximately 100 mm. Hg., while, at the tissue end, the oxygen pressure is only 19 mm. Hg. To understand the combination of oxygen and hemoglobin it is necessary to see how this reaction is effected by variations of the partial pressure of oxygen. The amounts of oxyhemoglobin and reduced hemoglobin that are formed according to the equation $\text{Hb} + \text{O}_2 \rightleftharpoons \text{HbO}_2$, at varying partial pressures of oxygen constitute the *dissociation curve of hemoglobin*. The dissociation of oxygen from hemoglobin is therefore dependent on the pressure of oxygen, but the dependence is not a directly proportional one. For example: the hemoglobin is completely saturated with oxygen at a pressure of 100 mm. Hg. The partial pressure can be reduced to 60 mm. Hg. without the freeing of much oxygen. When the pressure is reduced below 50 mm. Hg., the oxygen begins to be given off so rapidly that at a pressure of 10 mm. Hg., the hemoglobin has given up nearly all of its oxygen.

The dissociation curve for hemoglobin in human blood differs considerably from the curve determined on a solution of hemoglobin in a test tube. In other words there are factors active in the blood not present in synthetic solutions that conspicuously modify the reaction. These factors are the inorganic salt content of the blood, the temperature, and the reaction of the blood. The greater the CO_2 content, the more acid the blood reaction, the more readily is oxygen dissociation accomplished. The acidity is a very important factor in controlling the dissociation of oxygen and assuring the tissues an abundant supply of this necessary gas. At the tissue end of the circulation, where oxygen is most needed, the CO_2 tension is high and the dissociation of oxygen is facilitated. The effect of varying pressures of CO_2 on the dissociation curve of hemoglobin is shown in Fig. 3.

The Entrance of Oxygen into the Blood.—Arterial blood leaving the lungs is about 90 per cent. saturated with oxygen. The absorption of oxygen by blood fairly rich in CO_2 does not begin to lessen until the pressure of oxygen in the alveoli falls below 76 mm. Hg. The oxygen tension in the alveoli is approximately 100 mm. Hg. under normal conditions. This supplies a large margin of safety, and therefore the venous blood passing through the lungs leaves the lungs with an oxygen content near the saturation point under all ordinary conditions.

Haldane assigned to the cells lining the alveoli more than a passive role in the transfer of oxygen to the blood, believing that they actually secrete oxygen. He later modified this opinion and concluded that, under ordinary circumstances, the oxygen passes through the lung epithelium by simple diffusion; but that under certain abnormal conditions in which

FIG. 3



Dissociation curves of human blood, exposed to pressures of 0, 3, 20, 40 and 90 mm. CO_2 .
 Abscissa, oxygen pressure; ordinates, percentage saturation. (From J. Barcroft.)

the alveolar oxygen pressure is very low, these cells exhibit an active secretory activity. Many workers do not accept even Haldane's modified opinion, but regard the passage of oxygen through the epithelium under all circumstances as a process of simple diffusion. The matter must be regarded as unsettled.

The Passage of Oxygen Out of the Blood to the Tissues.—The actual carrying agent of oxygen in the blood, the red blood cell, does not come into very intimate contact with either the alveolar epithelium or the tissue cells. The oxygen reaches the red blood cell from the pulmonary epithelium and leaves the cells to reach the tissue cells by passing in solution through the plasma. There is a descending oxygen tension from red blood cells to plasma to tissue. The tissues absorb their needed oxygen from the plasma. The plasma then replenishes its oxygen supply from that contained in the red cells. The oxyhemoglobin of the red cells

therefore acts as a reservoir for keeping the oxygen tension of the plasma at a constant level.

The Administration of Oxygen.—The artificial administration of oxygen undoubtedly has great clinical possibilities which have never been fully used. It probably brings about its beneficial results by increasing directly the amount of oxygen that is absorbed in the plasma.

The Transportation of Carbon Dioxide by the Blood.—As a result of the oxidative processes taking place in the tissues, CO_2 is produced and the pressure of this gas in the tissues rises. This excess of CO_2 must be transported by the blood from the tissues to the lungs and there discharged from the body. As with oxygen, CO_2 is carried by the blood chiefly in a state of chemical combination. Arterial blood during rest contains 53 volumes per cent. of CO_2 at a pressure of 40 mm. Hg. Only 2.7 volumes per cent. are in simple solution, the remaining 50.3 volumes per cent. being in chemical combination (Haldane). It is as a weak acid, H_2CO_3 , that carbon dioxide enters into chemical combination with the blood. The blood contains an excess of alkali, chiefly sodium, above that combined with mineral acids. The carbonic acid is free to combine with this excess of alkali to form bicarbonate.

If an artificial solution of bicarbonate is made and its behavior to varying pressures of CO_2 is studied, it will be found to behave very differently than does blood. An artificial solution of bicarbonate is very stable and does not readily dissociate. At a CO_2 pressure as low as 4 to 6 mm. Hg. the artificial solution will give off little or none of its CO_2 ; even when exposed to a vacuum it will give up only about one-half of its CO_2 . Blood on the other hand at a CO_2 pressure only as low as 50 mm. Hg. will give off approximately one-half of its CO_2 , and when exposed to a vacuum, will give up practically all of this gas. It is clear therefore that if most of the CO_2 in the blood exists in the form of bicarbonate some modifying factor must be present. A clue to this factor can be had by studying the effects of the addition of a weak acid buffer, such as acid sodium phosphate, to the artificial bicarbonate solution. When such a buffer is added to the bicarbonate solution, the latter behaves exactly as does blood in response to varying pressures of CO_2 .

The blood contains but small traces of phosphate but does contain an abundance of a weakly acid substance which acts as a buffer. This weak acid is the protein, chiefly the hemoglobin, of the blood. If this view is correct, the mechanism of the behavior of CO_2 in the blood would be such that if blood were exposed to a vacuum, all the CO_2 it contained would be given off, and all the sodium would be in combination with the protein. As the blood was exposed to higher pressures of CO_2 , the weakly acid protein would yield its sodium to combine with the increasing amounts of carbonic acid to form bicarbonate. This explanation, which gives to the protein of the blood the role of a weak acid competing with the CO_2 for the alkali and enabling the CO_2 to be given up as the partial pressure of the gas falls, is the commonly accepted teaching. It is not the only theory, as Bayliss and Buckmaster have taught that hemoglobin and not alkali is the effective substance in the transportation of CO_2 . The evidence strongly favors the first explanation.

In discussing the role of alkali in the transportation of CO_2 , nothing was said as to the proportion of the CO_2 carried by the plasma and by the corpuscles. Both portions of the blood fix CO_2 . If corpuscles be separated from plasma and both portions be separately exposed to high concentrations of CO_2 , the corpuscles will contain the greater amount of the gas. If whole blood be first exposed to CO_2 and plasma and corpuscles separated after this exposure, the plasma will be found to have fixed the greater amount of CO_2 . The explanation of this somewhat anomalous experiment is that during the exposure of the whole blood, the hemoglobin withdraws the Cl ions of the plasma NaCl into the corpuscles, leaving behind Na , and thus increasing the available alkali of the plasma for the fixation of CO_2 . The hemoglobin is therefore the ultimate effective agent in the fixation of CO_2 both in the plasma and in the corpuscles. It accomplishes this not by directly uniting with the CO_2 but through its buffer effect as a weak acid.

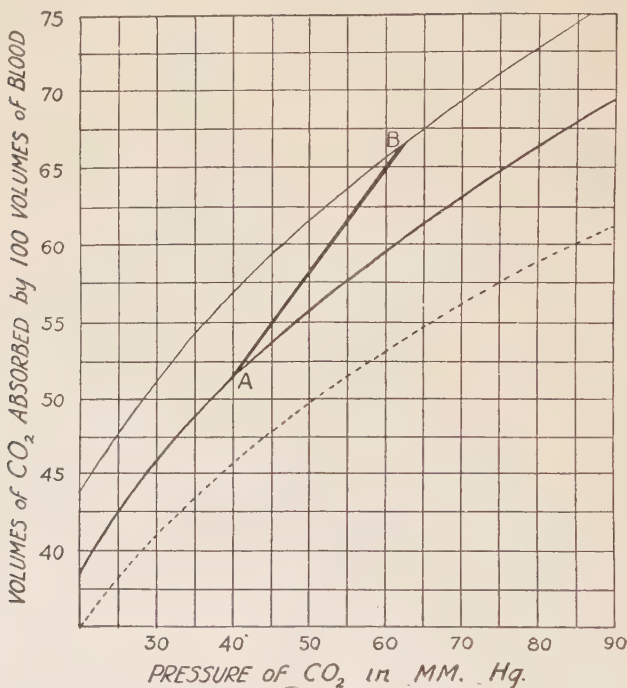
The Dissociation Curve of CO_2 .—This curve is constructed by determining the various volumes of CO_2 absorbed by the blood at increasing pressures of this gas. The curve is steepest in the lower ranges of pressure and tends to flatten out as the higher pressures are approached. The importance of this curve lies in the factors that modify it. The whole curve takes a lower level when determined in the presence of oxygen than when the determinations are made in the absence of oxygen. To state this more simply: blood takes up more CO_2 when oxygen is absent or when the percentage is low, and lowers its CO_2 content in the presence of higher amounts of oxygen (Fig. 4). This response of the dissociation curve is of great importance in the transportation and discharge of this gas. At the tissue end of the circulation where CO_2 must be taken up by the blood, the oxygen content is low and the absorption of the carbon dioxide is facilitated. Whereas in the alveoli, the discharge of the CO_2 is aided by the high oxygen content. It is probable that oxygen itself is not responsible for these effects but rather the amount of reduced hemoglobin.

The Discharge of CO_2 From the Body.—The discharge of this gas from the blood to the alveolar air is accomplished by simple diffusion. The relative pressures of this gas in the blood and in the alveolar air determine the discharge. In discussing the dissociation curve of CO_2 , it was shown that the amount of oxygen present was a responsible modifying factor.

Accommodation of the Body to the Changes in CO_2 Tension.—The respiratory centre is very sensitive to even minute changes in the CO_2 tension of the blood. Such acts as talking, swallowing, coughing, singing, etc., interrupt the steady elimination of CO_2 , yet there is little effect from the accompanying increase of CO_2 on the rate or rhythm of the respiratory acts. There are at least two factors that can be cited to explain how the respirations remain orderly in spite of the almost constant interferences occurring in the elimination of CO_2 . Haldane refers to these stabilizing factors as physiological buffers. The first of these buffers is the dead space air which dilutes any CO_2 that is temporarily prevented from escaping from the body. A second buffer is the lymph that surrounds the respiratory centre. Before the CO_2 tension of the centre can be effectively altered, the tension of the lymph must first be affected. This cannot

be accomplished quickly and thus alterations of the blood CO_2 are smoothed out and sudden changes in the CO_2 concentration of the respiratory centre are prevented.

FIG. 4



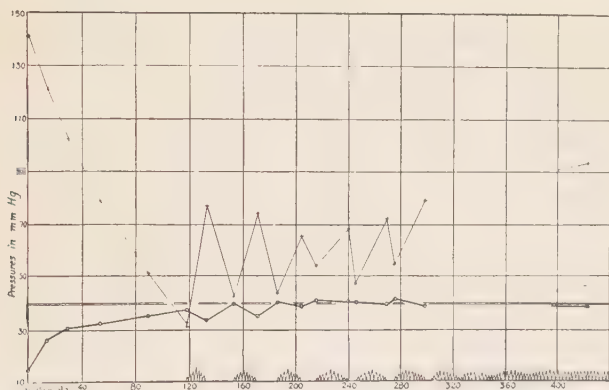
Curve to show CO_2 tension in blood, and the effect of the presence or absence of oxygen on this curve. Upper line shows CO_2 tensions when blood is shaken with CO_2 in the presence of inert hydrogen. Middle curve shows CO_2 tensions when blood is shaken with CO_2 in the presence of air. (The lower curve is to be disregarded.) The line AB represents the CO_2 tensions of the blood at pressures of CO_2 that exist within the body. At a tension of 40 mm. CO_2 —that present in alveolar air—the CO_2 of the arterial blood (A) is 52 vols. per cent. or approximately 6 per cent. lower than it would be in blood unsaturated with oxygen. At a pressure of 62 mm.—possibly present in the tissues—the venous blood contains 67 volumes per cent. CO_2 (B), or approximately 7 per cent. more than it would contain if the blood were saturated with oxygen (lower line). This shows how the high oxygen content of the blood at the lungs helps to drive off the CO_2 , and the low oxygen content at the tissues increases the blood's absorption of this gas. The abscissæ mark the tensions of CO_2 , the ordinates, the volumes per cent. of CO_2 taken up by the blood. (From MacLeod, after Christiansen, Douglas and Haldane.)

THE EXPLANATION OF SOME OF THE COMMON DISTURBANCES OF RESPIRATION

Cheyne-Stokes Respiration.—In this condition there are periods of apnoea alternating with periods of hyperpnœa. The change from one to the other is usually gradual and following the apnoea, shallow breathing is resumed which gradually deepens and quickens until marked hyperpnœa is present. It then lessens gradually until apnoea is again present. This typical picture is not always seen and there are many gradations and types of irregular breathing.

Cheyne-Stokes breathing may be divided into a physiological and a pathological variety. The *physiological* variety is seen in hibernating animals and occurs quite often during the sleep of normal infants. It may develop in healthy persons under a variety of conditions. Hypnotics, such as morphine and chloral, may induce it. It is most commonly seen at high altitudes and occurs in normal persons following a period of forced breathing. It is doubtful if there is any one common explanation for these occurrences. The explanation of the Cheyne-Stokes respiration following forced breathing has been worked out by Douglas and Haldane by studying the alveolar gases (See Fig. 5). They found that after forced breathing the alveolar air contains a high percentage of oxygen and a low percentage of CO_2 . With the blood gases in this pro-

FIG. 5



Curves showing variations in alveolar gas tensions after a two-minute period of forced breathing. The alveolar tension of oxygen is represented by the light line, the alveolar CO_2 tension by the heavy line and the normal alveolar CO_2 tension by the double line. The dotted line represents the alveolar CO_2 tension at which breathing would recommence at the end of apnoea with the alveolar oxygen pressures shown by the thin line. The dotted line really represents the irritability of the respiratory centre, a fall in this line indicating increased irritability. Actual breathing is indicated at the lower part of the figure. It will be seen that oxygen want is more important than excess of CO_2 ; for at times respiration begins before the alveolar CO_2 tension has risen to normal. (From Douglas and Haldane.)

portion there is no stimulus for further respirations. The over supply of oxygen is quickly used up, more quickly than the CO_2 accumulates. This lack of oxygen then stimulates the respiratory movements which again results in sweeping out the CO_2 and increasing the oxygen. This once more results in the cessation of respiration, and is repeated over and over. While this explanation is suitable for the Cheyne-Stokes breathing following deep respirations and for that occurring at high altitudes, it is not entirely satisfactory as an explanation of the periodic breathing seen in sleep and following the action of hypnotic drugs. It seems very likely that in these conditions there is a lessened irritability of the respiratory centre that interferes with the normal, regular respirations.

The *pathological* variety of Cheyne-Stokes breathing is seen in diseases of the brain, bloodvessels, kidneys and heart. The mechanism of the

respirations under these conditions is very complex, and there is no single explanation that satisfactorily fits all these conditions. It seems likely that insufficiency of oxygen, however caused, produces the irregular breathing. When it occurs after intracranial hemorrhage or in diseases in which intracranial pressure is raised, one explanation is that the systemic blood pressure fluctuates continually, and while it is less than the intracranial pressure, the respiratory centre is subjected to an oxygen supply less than its needs. The periodic breathing in cardiovascular disease probably results from a deficient oxygen supply to the respiratory centre for the administration of oxygen often alleviates it. A slowing of the whole blood stream or the local obstruction of vessels leading to the respiratory centre may account for its getting an insufficient amount of oxygen.

Respiration in Cardiac Disease.—Dyspnoea is perhaps the commonest symptom of heart disease. All cardiac patients, even those with but slightly diminished cardiac reserve, show a diminished tolerance to exertion as manifested by breathlessness. The complete explanation of this is still uncertain. It usually occurs in patients in whom there is passive congestion of the lungs which means that there is an exudate of fluid in the alveoli of a considerable area of the lungs. The functioning lung space is further decreased by cardiac hypertrophy and congested lungs are less elastic than normal lungs. These changes make pulmonary ventilation more difficult through mechanical interference. We know that pulmonary ventilation is accomplished at a disadvantage because the vital capacity is lowered. This is not, however, the whole explanation.

Another factor in the production of cardiac dyspnoea is the improper interchange of gases between the alveoli and the blood stream. Comparisons of alveolar and blood gases indicate a faulty interchange of carbon dioxide (Peters), and in some cases of extreme cardiac failure, an improper exchange of oxygen (Hurter and Harrop). Another possible factor in producing cardiac dyspnoea is deficient blood flow, although this has never been proved.

"Cardiac Asthma."—Another form of dyspnoea in cardiac disease is usually referred to as cardiac asthma. It differs from the usual dyspnoea of heart disease in that it is usually nocturnal in occurrence, is paroxysmal and its onset is unrelated to exertion. Its cause is now generally attributed to congestion of the pulmonary circulation incident to a sudden failure of the left ventricle.

The Response of the Respiratory System to Exertion.—When muscular exercise is undertaken, the demands for a greater supply of oxygen and for the removal of the excess of CO_2 are met by an increased blood flow and by a quickened rate of pulmonary ventilation. We wish to consider next how muscular exercise brings about the increased rate of pulmonary ventilation.

The first possibility is that the increased CO_2 produced as a result of exertion raises the alveolar CO_2 tension, and thus the hydrogen-ion concentration, and so stimulates the respiratory centre. However, increase in the alveolar CO_2 tension is not the cause; for it is never found increased sufficiently to account for the increased breathing. As a rule the alveolar CO_2 increases as the exertion increases but not sufficiently to account for

the degree of hyperpnœa that is brought about. When the exertion becomes extreme, or if the subjects are "untrained," the alveolar CO_2 pressure actually falls. In observations made on himself, Haldane found that his alveolar CO_2 pressure never rose appreciably with exertion; it actually fell if the exercise was at all strenuous, provided ordinary air was breathed. On the contrary if oxygen-rich air was breathed during the exertion, there was a well-marked increase in the CO_2 tension of the alveoli. This and other evidence led to the belief that the increased breathing of exertion is due to anoxemia or insufficient oxygen. The formation of excessive lactic acid during exercise could explain the respiratory behavior but lactic acid is only produced in the absence of sufficient oxygen. While this latter factor may be in part responsible, on the whole, anoxemia is the most likely and least confusing explanation of the respiratory behavior in response to exertion.

We must next discuss in brief the way in which anoxemia is brought on by exercise. Barcroft has suggested as an explanation that owing to the increased rate of blood flow there is insufficient time for the completion of the chemical reaction between the inspired oxygen and the hemoglobin of the blood. Haldane believes that when there is an excessive need of oxygen, the lung epithelium actively secretes oxygen, and not merely acts as a passive secreting membrane as it does when the oxygen requirements are normal. This property of the respiratory epithelium can be increased. The abatement of the unpleasant respiratory accompaniments of strenuous exertion that follows "training," Haldane believes to be the result of an increased development of this secretory action by the lung epithelium. Haldane's explanation is probably the most generally accepted one but objections to its correctness can be and have been raised.

Pulmonary Emphysema.—In this condition the lungs approximate a state of inspiration, with but slight excursions during inspiration and expiration. The total volume of the lungs is increased but there is a loss of elasticity and a decrease in functioning alveolar surface. These changes result in an improper exchange of gases between the alveolar air and the blood. On examining the alveolar air the oxygen tension is often found to be considerably lower, and the CO_2 tension considerably higher, than normal. In spite of this there is as a rule surprisingly little breathlessness at rest. The reason for this apparently anomalous condition probably lies in the fact that the condition has developed insidiously and time has given the body an opportunity to develop certain compensatory factors. One of these is polycythemia which increases the blood's capacity for absorbing oxygen. There is also apparently a compensatory mechanism developed to care for the increased CO_2 in that the alkali reserve is increased so that the hydrogen-ion level is maintained in spite of the increased CO_2 . These factors render the emphysematous subject fairly free from dyspnœa at rest, but they fail to compensate when exertion demands an increased pulmonary ventilation.

Lobar Pneumonia.—The greatest cyanosis and distress in breathing come early in the course of the disease. Studies on the gases of the blood at this stage give an adequate explanation of the dyspnœa early in pneumonia. Both a low oxygen content and CO_2 retention are found. This is

believed to result from non-functioning due to pain and involvement of areas of the lungs, sufficiently extensive to cause a pollution of the general circulation with under-oxygenated blood in spite of the increased ventilation of the uninvolved portions. Later in the disease this pollution does not occur because the circulation through the consolidated lungs is entirely shut off. If the blood gases are studied after this has occurred, the CO_2 content is found to be low, and the oxygen content high. Under these conditions there is no adequate chemical basis upon which the continued increased breathing can be explained. One explanation suggested is that the toxins of pneumonia exercise a specific stimulating effect on the respiratory centre. Meakins has shown the inadequacy of this explanation by pointing out that were this so, we should see increased breathing in pneumococcic infections occurring elsewhere in than the lungs. Another suggestion is that the inflammatory processes in the alveoli upset the Hering-Breuer reflex, and thus bring about dyspnoea much as may minute pulmonary emboli. It seems not unlikely that this explanation may have some truth in it.

Bronchopneumonia.—In bronchopneumonia cyanosis and dyspnoea are present as in lobar pneumonia. Their presence is due to the continued low oxygen and high CO_2 content of the blood. This state results because the circulation to the many small pneumonic areas is not shut off, and the blood leaving these areas being under-oxygenated, returns to the left heart rich in CO_2 and low in oxygen.

Pulmonary Tuberculosis.—In this disease there is notoriously little breathlessness and cyanosis, the reason being that as the pulmonary process progresses the circulation to the affected portions is shut off. Poorly oxygenated blood is thus prevented from entering the general circulation.

OBSTRUCTIONS WITHIN THE RESPIRATORY TRACT

Laryngeal and Tracheal Obstruction.—When an obstruction in this portion of the respiratory tract develops fairly suddenly, the rate of breathing is first slowed and the depth increased. The respirations soon become shallower and more rapid, marked cyanosis appears, and eventually respiration ceases. These respiratory phenomena are undoubtedly due both to an acute oxygen want and to an accumulation of CO_2 , or, as it is expressed, the respiratory failure is both of the anoxemic and asphyxial type. If the obstruction develops more insidiously and the obstruction is not complete, absolute respiratory failure does not occur; the tissues of the body develop some compensatory mechanism against the chemical changes occurring in the blood.

Bronchial Obstructions.—This subject may be considered under the heads of diffuse and localized obstructions. Bronchial asthma is an example of diffuse, and a foreign body of localized obstruction.

Bronchial Asthma.—The typical attack is accompanied by great respiratory distress, particularly during the expiratory phase. The paroxysm is due to a narrowing of the lumen of the bronchioles, brought about by spasm or oedema of the bronchial musculature, and by the exudate that

is poured into the lumen of the bronchioles and alveoli. The explanation of the expiratory difficulty is that during normal inspiration there is a tendency for the elastic lung tissue to expand the bronchioles and oppose a contracting action of their musculature. Even during a spasm of these muscles, this force overcomes the spasm sufficiently to render the entrance of air easy. During expiration, however, there is a relaxation of all lung tissue and the spastic bronchial muscle is unopposed. When the expiratory muscles act violently, as they do in asthma, this aids in the constriction of the bronchioles and adds to the difficulty of expiration.

In asthma there is a definite anoxemia resulting from a faulty ventilation of some of the alveoli. There may be an associated retention of CO_2 . Both these chemical factors have a role in the causation of the dyspnoea. If only a relatively few alveoli are non-functioning, the increased breathing will sweep off the excess of CO_2 . With this the dyspnoea ends, only to recur as the CO_2 tension of the blood again increases. This gives the appearance of a periodic or paroxysmal asthma, whereas in reality the asthmatic seizure has never been ended; the CO_2 tension of the blood has only been lowered temporarily. If a larger number of alveoli are non-functioning as a result of bronchial spasm, the resulting dyspnoea will not succeed in sweeping out the excess of CO_2 , the increased, labored breathing continuing until the spasm of the bronchial muscle is ended.

Foreign Bodies.—The commonest cause of localized bronchial obstruction is a foreign body. The inspired foreign bodies do not always bring about so complete an obstruction as to cause collapse of the whole or a portion of a lung. The obstruction may be such as to cause expiratory retention. However, as inspiration expands the lungs, the bronchi are expanded sufficiently to allow air to pass the obstruction and reach the lungs distal to the obstruction. Expiration however, narrows the lumen of the bronchi, increases the obstruction, and prevents the inspired air from escaping. This causes an emphysema of the lung or of that portion which is supplied by the obstructed bronchi. Local emphysema is a valuable sign of non-opaque foreign bodies.

The respiratory accompaniments of foreign body will depend upon the amount of obstruction, collapse, and the amount of secretion and infection that result. If these all combine to render any considerable portion of a lung non-functioning without shutting off the circulation to the involved portion, the general circulation will be polluted with under-oxygenated blood and dyspnoea and cyanosis will result. If the result of the foreign body is a small localized emphysema, there will be no dyspnoea or cyanosis at rest.

Collapse of Lung.—We will refer briefly to the collapse seen in pneumothorax and to the collapse seen in the condition generally referred to as massive collapse of the lung.

Pneumothorax.—In this condition the lung collapses because the normal negative pressure in the intrapleural space is replaced by a positive pressure. Following such a collapse, the circulation to the collapsed lung is completely shut off. If the remaining uncollapsed lung is sufficiently healthy, it can adequately take care of the necessary interchange of gases between the outside air and the blood. Because of this and because the

circulation that cares for the gaseous exchange goes only to the normally functioning lung, the blood is not polluted with under-oxygenated blood and there is no respiratory distress at rest. When even moderate exercise is undertaken, however, the one functioning lung is not able to care for the gaseous needs and distress occurs. This statement refers to an uncomplicated or artificially induced pneumothorax. If lung disease is the cause of the pneumothorax, the respiratory picture may be modified by the disease.

Massive Collapse of the Lung.—This condition is usually a postoperative occurrence or due to a foreign body completely plugging a bronchus. It is only in recent years that the condition has been clearly identified. Formerly most examples of this condition were considered to be postoperative pneumonias. The signs seen in complete collapse are a marked displacement of the heart toward the affected side, a high diaphragm on the collapsed side, and dulness on percussion. In a number of these cases, the cause of the collapse has been shown to be a complete obstruction of a bronchus by a plug of mucus. The explanation of the displaced heart and high diaphragm on the affected side is that the air trapped in the lung by the obstruction is absorbed and the lung, as a result, contracts. This greatly increases the negative intrapleural pressure which, in a sense, pulls the diaphragm up and the heart over. Another factor is assumed to be the cause by some observers, who believe that a primary paralysis of one side of the diaphragm is responsible. It is difficult to say which of these two explanations is correct. There may be truth in both.

When the collapse is complete, the circulation is probably shut off and theoretically there should be no great respiratory distress. Actually, however, there usually is. Other factors may contribute as infection usually follows upon the collapse and the subjects of postoperative collapse are generally in a weakened, shocked condition. Moreover the distorted position of the heart seriously interferes with its action.

The Effort Syndrome.—In this condition the breathing may be quickened at rest. Characteristic of this syndrome is a very excessive quickening of the breathing in response to very moderate exertion. The respirations are not only rapid but shallow as well. Haldane and his associates concluded that the syndrome was due to an abnormal increase in the readiness with which the Hering-Breuer reflex was elicited. In other words they believed that it was due to a reflex restriction of the depth of breathing. After studying farther the matter of fatigue of the respiratory centre, they modified their views and concluded that the rapid, shallow breathing was not due to any increase in the strength of the Hering-Breuer reflex, but rather to a weakening in the persistence of the individual inspiratory and expiratory discharges from the centre. In other words, the causative change is a weakening or fatigue of the respiratory centre and not a change in the nervous impulses that make up the Hering-Breuer reflex.

Breathing in Rarefied Air.—When we study the effects of this we are studying the effects of anoxemia brought on by a low oxygen tension in the atmospheric air. The best example of the effects of the anoxemia induced by breathing rarefied air is the train of symptoms that go to

make up the condition known as mountain sickness. These symptoms vary in different individuals. Nausea, vomiting, headache and various mental manifestations, almost always including depression, are usual. These may develop after a varying length of exposure to the low oxygen tension. Indeed their appearance may be delayed until the exposure to the low atmospheric oxygen pressure has been ended. Once having appeared these symptoms may continue for a considerable time after a return to a normally rich oxygen atmosphere.

The condition itself is relatively trivial. Its importance lies in its illustration of the wide-spread effects that even slight degrees of anoxemia may have. It is probable that no single body cell fails to feel the effect of even slight degrees of oxygen want. Even though the anoxemia be slight, permanent damage will be done if the anoxemia is not ended or if compensatory mechanisms do not develop to alleviate it.

The respiratory responses to the anoxemia induced by breathing rarefied air are those seen in anoxemia otherwise induced. There is mild dyspnoea especially on exertion. This results in the blowing off of CO_2 and the lowering of the alveolar CO_2 tension. Evidences of an alkalosis rather than an acidosis are seen in the absence of an increased lactic acid formation, and diminution in the excretion of urinary acid and ammonia. It has been pointed out that the kidneys play a leading role in compensating this disturbed acid base balance, and that the compensating process is a slow one. It therefore would require a considerable time for the alveolar CO_2 tension to reach its ultimate low point if exposure to the low oxygen tension were continued, or to return to its normal level after the restoration of a normally rich oxygen atmosphere. In this way the continuance of the symptoms of mountain sickness after a return to a normal oxygen tension can be understood.

After one has lived for some time in rarefied air, the symptoms of mountain sickness no longer manifest themselves; an acclimatization takes place. Haldane's explanation of this acclimatization is that the lung epithelium develops a secretory action, so that oxygen no longer enters the blood by simple diffusion but is actively transferred by secretion. The alternative explanation is that acclimatization is accomplished through the development of three compensatory processes: (1) an increase in the amount of hemoglobin and the number of red blood cells; (2) an increased affinity of hemoglobin for oxygen; and (3) an increased pressure of oxygen in the alveolar air brought about by the increased pulmonary ventilation.

Breathing in Compressed Air.—If one who has been in an atmosphere of compressed air returns to atmospheric pressure too quickly, very serious symptoms may develop. These are severe muscle and joint pains, motor paralyses, respiratory and cardiac failure. So common was this condition among divers and caisson workers before preventive precautions were discovered, that the syndrome is still known as caisson disease or diver's palsy.

The explanation of the occurrence of these symptoms is that during exposure to the increased pressure of compressed air, the blood absorbs large quantities of nitrogen gas. This occurs because of the law that the

amount of gas that a liquid will absorb is directly dependent upon the pressure of the gas. Symptoms do not occur until the excessive atmospheric pressure is reduced. When this is accomplished too quickly, the excess of gas in the blood and tissues is released from solution and forms gas bubbles which act as air emboli. Equalization of the gaseous tension of the blood and tissues with that of the outside air cannot be accomplished immediately. These symptoms may be prevented by restoring the atmospheric pressure gradually. If this is done the gaseous equilibrium between the blood and the outside air is successfully restored.

Anemia.—In anemia there is often a reduction of the hemoglobin of the blood by more than 50 per cent. This leaves the blood with considerably less than one-half of the substance responsible for the active transportation of oxygen. Under these circumstances, one might expect anoxemia to occur. Such is not the case, however. A constant evidence of anoxemia is a low alveolar CO_2 tension. In anemia this is not present. Haldane believes that the low oxygen carrying power of the blood is compensated for and anoxemia avoided by an increased rate of circulation.

CHAPTER II

DISEASES OF THE NASOPHARYNX, PHARYNX, AND TONSILS

By FRANCIS R. PACKARD, M.D.

ACUTE NASOPHARYNGITIS

Etiology.—Acute inflammations limited strictly to the nasopharyngeal region are of rather rare occurrence and are usually exacerbations of a chronic inflammatory condition. The mucous membrane of the nasopharynx being continuous with that lining the nose is almost always more or less involved in inflammations of the Schneiderian membrane, and frequently after the rhinitis has disappeared, the nasopharyngitis which has been associated with it remains. Occurring primarily, acute nasopharyngitis is generally the result of exposure to cold or damp. It is very apt to follow sudden changes in temperature and is occasionally seen in connection with digestive disturbances. It sometimes arises from the inhalation of irritant vapors or dust. It is apt to occur in conjunction with or following acute infectious diseases, such as scarlet fever and diphtheria.

Pathology.—The manifestations are of those of acute catarrhal inflammation of the mucous membrane. There is the usual stage of acute engorgement of the bloodvessels, followed by increased glandular activity with profuse secretion. The inflammation either subsides by the ordinary processes of resolution or assumes a chronic form.

Symptoms.—The first complaint is generally of a sensation of discomfort in the back of the throat. At first there is a dry cough; after some days the secretion, which is at first clear and white, becomes thick and mucopurulent and may be quite profuse. The attack is apt to be attended with slight fever, the temperature rising to 101° F. Occasionally the patient complains of tinnitus and a sensation of fulness in the ears owing to occlusion of the pharyngeal extremities of the Eustachian tubes.

Treatment.—Nothing affords more comfort than douching the nasopharyngeal space with warm normal salt solution or with a warm alkaline antiseptic solution. This may be accomplished by allowing the patient to snuff up the solution through the nares or by the physician injecting the solution into the nasopharynx by means of a postnasal syringe. Should the patient complain of much sore throat and pain, it is comforting to inhale hot medicated vapors. For this purpose nothing is more satisfactory than the compound tincture of benzoin. After cleansing the nasopharynx, great lessening of the congestion will be produced if a solution of nitrate or an albuminate of silver is applied on a cotton pledget directly to the mucous membrane. The nasal passages should be kept

open in order that respiration may be free, and for this the local application of epinephrine solution (1 to 5000) is useful. This should be followed by the use of a bland oil spray containing a little camphor and menthol.

CHRONIC NASOPHARYNGITIS (POSTNASAL CATARRH)

Etiology.—Chronic nasopharyngitis may be the result of repeated attacks of acute nasopharyngitis. More usually, however, frequent acute attacks of nasopharyngitis are the manifestations of an underlying chronic inflammatory condition. Chronic nasopharyngitis is very commonly associated with gastro-intestinal disturbances. It is a frequent sequel of acute infectious diseases, especially influenza, scarlet fever, and diphtheria. The abuse of alcohol is a common cause, chiefly because of the digestive disturbances caused by it. Chronic nasopharyngitis frequently results from, or, if it exists, is kept up by the abuse of tobacco. Intranasal deformities, or chronic obstructive conditions within the nose, often cause the pharyngeal mucous membrane to become inflamed, and the condition continues until the cause is removed. Of the direct causes of chronic nasopharyngitis, the most common is exposure to a damp climate in which the patient is subject to sudden variation of temperature. Thus it is especially prevalent near the Atlantic seaboard of the eastern United States. Occupation is frequently not only a predisposing but also an exciting cause when it exposes the patient to the inhalation of irritant vapors or dust.

Symptoms.—The most characteristic symptom is the sense of irritation which is almost constantly present in the nasopharynx, causing the patient to have a tendency to hawk, in an effort at relief. This only serves to irritate the inflamed structures yet further. Frequently the patient's throat becomes so sensitive and the irritation so great, that retching or even vomiting results. The patient complains of continuous postnasal dropping of mucus. There is, as a rule, not very much secretion to expectorate, such as there is being thick, tenacious, and slimy. In advanced cases the discharge is apt to be mucopurulent and greenish, and occasionally we see the formation of crusts and scales, which are apt to be somewhat blood-stained because of abrasion of the mucous membrane. The secretion in the postnasal space frequently undergoes decomposition and renders the breath offensive. The voice is generally husky and without the proper resonance. There are very apt to be aural disturbances, sometimes of quite marked severity, because of obstruction of the pharyngeal orifice of the Eustachian tube, occasionally from the extension of the inflammation up the tube, and at times because of the nasopharyngeal secretion entering the tube. The mucous membrane of the pharynx or larynx may show catarrhal changes. Disturbances of digestion are very common, generally taking the form of dyspepsia. On examination the nasopharynx will be seen to contain a quantity of thick stringy secretion, upon the removal of which the mucous membrane will present a dry, glazed, and congested appearance. Sometimes there is considerable swelling so that it is hard to inspect the upper portions of the postnasal space.

Treatment.—Of all the measures, none are more efficacious than those which deal with general hygiene. The clothing should be regulated in order that the patient's bodily temperature may be kept as even as possible. For this purpose he should wear, both winter and summer, some form of mesh underwear. Undergarments of this character permit free evaporation of the perspiration and do much to further the activity of the skin and to prevent evaporation. If the patient is able to stand a cold tub bath every morning it will greatly promote the circulatory activity of the skin. If he cannot take the plunge or shower bath, he may at any rate douche his neck, shoulders, and chest with cold water. Careful instruction should be given as to the proper ventilation of his bed-room, as these patients are very apt to form an idea that "taking cold" is promoted by night air, and hence they exclude it. If the patient leads too sedentary a life, some regular form of exercise should be insisted upon. Dietetic errors should be corrected, and the use of tobacco and alcohol regulated, or, if necessary, interdicted.

The patient should be given an alkaline antiseptic douche, with directions to snuff it up through the nostrils into the nasopharynx, following which he should be directed to use a bland oil spray. Locally there are many substances which prove of value, their usefulness varying greatly in different cases. At least two or three times a week, at the commencement of treatment, the physician should thoroughly cleanse the nasopharynx, and apply some astringent or alterative preparation to the inflamed mucous membrane according to the indications present. For thorough cleansing it will generally be found necessary not only to use a solution through the anterior nares, but also to wash out the nasopharynx with some form of postnasal syringe. Any of the ordinary alkaline antiseptic solutions may be used, such as Dobell's solution, or those which are made up as the various so-called antiseptic nasal tablets. Should the secretion in the nasopharynx be offensive, a weak potassium permanganate solution used as a douche often gives a gratifying results. After the muco-pus which has collected in the postnasal space has been removed, nitrate of silver in a solution of 30 to 60 gr. to the ounce may be applied with cotton on an applicator, or one of the many preparations of albuminate of silver may be used.

HYPERTROPHY OF THE LYMPHOID TISSUES IN THE NASOPHARYNX. ADENOID GROWTHS IN THE NASOPHARYNX. HYPERTROPHY OF THE PHARYNGEAL TONSIL

This condition is really a hypertrophy of the glandular tissue which normally exists to a greater or lesser extent in the vault of the pharynx, in other words, of the tissue generally known as the "pharyngeal tonsil." The term "third tonsil" is frequently applied to these adenoid vegetations. The etiology is obscure. It undoubtedly occurs most commonly in conjunction with enlargement of the faucial tonsils, and used to be referred to as one of the manifestations of the "lymphatic diathesis." Although it occurs with marked frequency in children who suffer from tuberculous or syphilitic taint, it is, nevertheless, seen in the children of

healthy parents, and it would seem more rational to consider its presence in children with tuberculosis or syphilis, as a result of the anemia attendant upon those diseases rather than as a manifestation of the disease itself.

Climatic conditions undoubtedly exercise an influence; thus the condition is much more frequent in low, damp localities in which there are frequent changes of temperature than it is in better climates. It is doubtful if the condition is ever congenital, although a condition of nasal catarrh is often noticeable in young infants in whom there is a subsequent development of adenoid vegetations in the nasopharynx. Kyle held that the cause of the so-called inherited tendency to adenoids is frequently found in the inherited family nose, the hypertrophy of the glands in the nasopharynx being more common in children whose nostrils have a narrow slit-like orifice than in those whose nostrils are wide open. In both children and adults this glandular hypertrophy is frequently found in association with hypertrophic rhinitis.

Pathology.—Adenoid vegetations in the nasopharynx are generally composed of a mass of hypertrophied lymphoid glandular tissue, covered with epithelium. Farther down in the structure, there are ramifying trabeculae of connective tissue with lymphoid cells lying between them. The proportion of lymphoid to connective tissue varies greatly in different specimens, thus, in very young children who have not been subject to repeated inflammatory attacks or congestion of the tissue, the structure is soft and the glandular lymphoid element predominates. In older patients the vegetations have usually been the site of various local congestive and inflammatory changes which have resulted in the deposit of inflammatory material with overgrowth of connective tissue and consequent hardening of the structure. The surface of these growths is generally very markedly lobulated or mammillated.

Symptoms.—The most prominent symptoms are those which arise from nasal obstruction, and of these the most striking is the appearance of the face which results from habitual mouth breathing. Everyone is familiar with the aspect of the unfortunate beings who are unable to respire properly through the nose. The dull, expressionless face, lack-lustre eyes, wide-open mouth, with protruding upper lip, and hanging lower jaw, accompanied by an inability to fix the mind upon a task, and the general stupidity and mental dulness frequently lead to their being regarded as mentally deficient. In fact, it is this mental sluggishness to which Guye, of Amsterdam, gave the term "aproxexia." There is also often an associated deficiency of hearing, the result of obstruction of the pharyngeal orifices of the Eustachian tubes. This deafness adds materially to the child's apparent stupidity. These children are rendered more unattractive by the fact that they are generally irritable and cross because of their constant physical discomfort.

The obstruction to nasal respiration is almost invariably most marked at night when the circulation is more sluggish, and mucus more apt to accumulate. This results in restless and disturbed sleep, and frequently in nightmares whereby the child is deprived of natural slumber, and the discomfort is materially aggravated. Quite often the patient is brought

to the physician because of restlessness at night, and for the snoring and grunting which are so noticeable at that time. As a result of the air not being moistened and warmed by its passage through the nasal chambers, patients who suffer from adenoids are also frequently subject to inflammation of the pharynx and larynx, or even to attacks of bronchitis. In this way adenoids are probably the most common predisposing factor in asthma and spasmodic croup in young children. The child's voice is affected at a very early stage and in a very characteristic manner. The loss of nasal resonance alters the character of the voice. There is generally considerable mucus discharge from the nose, and a lack of ability to properly expel this causes the child to keep up a continuous sniffing.

Of all the evil results which adenoids may produce, there are none more serious than those which occur in the *ear*. The aural complications vary greatly as regards their manifestations and their seriousness. There may be attacks of pain due to interference with the patency of the Eustachian tube on the affected side. This same obstruction, however, frequently leads to serious results in the middle ear, the result of constant interference with its proper ventilation through the Eustachian tube, giving rise to chronic catarrhal otitis media, and leading to impairment of the hearing. More serious is the constant liability to infection of the middle ear. The vegetations are always swarming with microorganisms, and there is no doubt that their proximity to the Eustachian tube frequently permits of their access to the middle ear.

Children with adenoids are often subject to repeated attacks of inflammation of the fauces, pharynx and faucial tonsils. As a result of these, there is apt to be enlargement of the lymph glands in the cervical region. The presence of adenoid growths in the nasopharynx is also frequently responsible for the maintenance of a chronic catarrhal conjunctivitis. Peculiarities in the formation of the hard palate, and various irregularities of the teeth are also in many instances to be attributed to the interference with nasal respiration.

Diagnosis.—This generally gives but little difficulty. The peculiar facial expression and the history suffice in many instances to make the condition plain. Examination by posterior rhinoscopy is frequently a difficult matter in children, but enough can be usually be seen with a mirror to justify the diagnosis, if the vegetations are present. Digital examination of the nasopharynx is painful, and it is to be avoided unless deemed absolutely necessary.

Treatment.—This consists solely in the removal of the adenoid mass, the only questions being as to the suitable time, the method to be used, and the anesthetic to be employed. Although their presence in sufficient amount to produce serious symptoms always demands their removal, nevertheless, the demand is not so urgent as to interfere with the surgeon delaying the operation until the patient shall be in the best condition for it. The general health is apt to be considerably below par, and it is well to give a little time to building up before the operation is performed. It should not be done while there is any acute inflammatory condition in the air passages or ears, as the existing condition will almost invariably

be aggravated. The removal of adenoids is preferably done with the patient under the influence of a general anesthetic. For this purpose ether is to be preferred. The child should be placed in a supine position with the head hanging over the operating table in such a manner that the blood will tend to flow out through the mouth instead of down into the larynx, or a modified Trendelenburg position may be used. The mass may be removed with an adenotome, a Gottstein curette, or one of its numerous modifications, or with the forceps designed by Lowenberg. Should disease of the faucial tonsils be associated, the latter should be removed while the patient is under the anesthetic and just before the removal of the adenoids is undertaken.

DISEASES OF THE PHARYNX

The pharynx possesses the unique distinction of forming a portion not only of the upper air passages but also of the digestive tract. This renders its mucous membrane very susceptible to influences and conditions which affect that of the digestive tract. Thus, disorders of digestion and assimilation are very apt to be accompanied by pathological changes in the pharynx. The expression "stomach cough" is not, in many instances, an improper one to apply to the cough which accompanies a congestion of the pharynx due to digestive derangement. The continuity of the pharyngeal mucous membrane with that of the rest of the respiratory tract leads to its frequent involvement in conditions affecting the integrity of the latter. Any obstruction to nasal respiration is apt to be productive of serious inflammatory changes in the pharyngeal mucous membrane. Such nasal obstruction causes the inspired air to pass directly into the pharynx without having been warmed and moistened by previous passage through the nostrils. Consequently, from the air taking up its moisture, the surface becomes dry, congested, and predisposed to inflammatory changes. It is this factor fully as much as its continuity of structure that causes the pharyngeal mucous membrane to share, as a general rule, in any inflammatory disorder of the nose or nasopharynx.

ACUTE PHARYNGITIS

Etiology.—This occurs but rarely as an exclusive entity. It generally coincides with an acute digestive disorder or is an exacerbation of a chronic inflammation of the pharyngeal mucous membrane. Owing to its very exposed position, it is remarkable that the pharynx is not more frequently the site of pathological changes. The commonest cause is exposure to wet or cold, or rapid changes of atmospheric temperature. It also occurs in conjunction with acute digestive disorders. Excessive smoking frequently excites an attack.

Symptoms.—The symptoms are not, as a rule, very marked or severe. There is a "raspy" feeling or soreness, sometimes true pain in the pharynx.

geal region, occasionally extending up along the Eustachian tubes. Swallowing is usually painful, and there is more or less cough, accompanied by a small amount of thick mucopurulent expectoration. The attack may be ushered in by chilly sensations, and slight malaise and mild fever usually attend it, as do also occasionally general pains and constipation. On inspection, the pharyngeal mucous membrane is seen to be red and somewhat swollen. At first the surface is dry and glazed, but as soon as secretion is established there is much more discharge. Frequently there is marked prominence of the small bloodvessels on its surface. There is almost always also considerable redness of the fauces and tonsils.

Treatment.—In almost every instance it is better to begin this by free purgation. This is particularly beneficial if we use calomel followed by a saline. The salicylates exert an almost specific influence in most attacks. If the patient's stomach is upset, or during the period when calomel is being given, it is better to let him take 5 gr. of salol every two hours rather than the more powerful (but at the same time more irritant) salts of salicylic acid. Locally, great relief will be experienced from the use of various lozenges or gargles. If the mucous membrane is very dry and glazed, a lozenge of chlorate of potash is often most useful. If the pain is intense cocaine lozenges often afford relief. A lozenge containing camphor and menthol is also useful in allaying the severe irritation. Sucking cracked ice lessens the congestion and gives great comfort. Although gargles are not as efficient as direct applications to the parts, nevertheless, a bland antiseptic gargle, such as Dobell's solution or normal salt solution, is often very grateful and relief often follows the use of a 1 per cent. solution of acetyl salicylic acid. If the congestion of the mucous membrane is very marked, it is well to paint the surface with a strong solution of nitrate of silver (30 to 60 gr. to the ounce; 2 to 4 gm. to 30 cc.), or with an albuminate of silver solution. A very strong solution of silver nitrate not only acts as an astringent but is an antiseptic, and to a certain extent an analgesic. The patient should be confined to one room, if not to bed. He should be placed on a light diet, and forbidden to smoke or use alcohol. He should likewise use his voice as little as possible.

CHRONIC CATARRHAL PHARYNGITIS

Etiology.—This common affection is particularly apt to occur in those whose occupation requires constant use of the voice, hence it is frequently termed "voice user's" or "clergyman's sore throat," when it is generally accompanied by laryngitis. In such persons it occurs usually as the result of straining the voice, particularly by using it in a faulty manner or at times when there is some inflammation of the parts concerned. Other local factors are the use of tobacco, and the inhalation of irritant substances such as the fumes of acids or alkalies, and other gases. Chronic pharyngitis frequently results from catarrhal affections of the nose, most generally because of nasal obstruction causing mouth breathing. When there is considerable dropping of mucus in the back of the throat from nasopharyngitis, the pharyngeal mucous membrane becomes inflamed

and irritated not only from the direct action of the secretion, but because the efforts to expel the mucus cause congestion of the entire pharyngeal wall.

Chronic pharyngitis is frequently seen in association with chronic diseases of the liver, kidney, and heart, as a result of passive congestion. It is one of the commonest manifestations of chronic alcoholism.

Pathology.—In the early stages there is a general hyperemia. Later, the membrane becomes thickened, and there is marked increase in the connective tissue elements, with the formation of prominent granulations. The process, as a rule, does not markedly involve the glands in the mucous membrane. In many instances the engorgement of the bloodvessels is the most prominent feature.

Symptoms.—The chief subjective symptom is a cough which is irritable, unproductive, and easily excited by change in atmosphere. The mucous membrane of the throat is red and congested, with considerable dry, slimy mucus adherent to its surface. The voice is generally quite markedly changed, there being considerable huskiness and the patient may at times lose the voice almost completely. A curious complaint is of a frequent desire to swallow; occasionally swallowing is accompanied by pain. There is engorgement of some of the bloodvessels.

Treatment.—This should first be devoted to the underlying cause. If this is found to be a faulty use of the voice, the patient should be given instruction to correct this. The closest attention should be paid to the condition of the digestive tract. Even if the pharyngitis is not dependent upon a disordered digestion, the latter is apt to be associated with it, and its correction is an important factor. The habits, as regards tobacco and alcohol, should be carefully noted. Locally, an alkaline antiseptic wash, such as Dobell's solution, should be used as a spray. For cleansing purposes it will be found much more efficacious if the upper portion of the throat is sprayed out through the nostrils in addition to the direct spraying of the pharyngeal mucous membrane. Frequently, gargling with warm salt solution is found more agreeable and efficient than the use of solutions through the atomizer. The local application of a strong solution of nitrate of silver (30 to 60 gr. to the ounce) daily, or every other day, is a useful adjuvant.

CHRONIC FOLLICULAR PHARYNGITIS

This is characterized, as contrasted with the preceding, by the marked involvement of the glandular elements in the pharyngeal mucous membrane. This produces a granular appearance which has caused the term "follicular." Its etiology is, in most instances, similar to that of chronic catarrhal pharyngitis. Following attacks of acute infectious diseases, such as scarlet fever and diphtheria, a chronic follicular inflammation of the pharyngeal mucous membrane is quite frequently left. Swelling or hypertrophy of the submucous glands on the posterior wall of the pharynx is frequently the result of infection from adenoid growths in the nasopharynx. Such glandular involvement may continue after the removal of the source of infection by operation. Sometimes the swollen glands are few in number or even solitary and may give rise to the sus-

picion that they are neoplastic. More frequently they present themselves as multiple elevations.

Symptoms.—The subjective symptoms are usually much more noticeable than in a simple chronic catarrhal pharyngitis. There is generally more cough and the voice is much hoarser. The cough is unproductive, except for occasional sticky masses, which are dislodged with difficulty. The pain, which is apt to be a particularly disagreeable feature, is of an aching character, and sometimes very sharp. Upon examination, the posterior pharyngeal wall is seen to be dry and glazed, and of a reddish color; scattered across its surface are numerous prominent granulations. There is usually a scanty amount of mucus present upon it and one or more submucous glandular swellings.

Treatment.—This must be directed especially toward the correction of any underlying diathesis or constitutional cause. The hygiene of the patient's daily life must be carefully inquired into, particularly as to his habits regarding alcohol and tobacco. If he is a voice user, he should have instructions as to the proper method for its employment. The stimulation of the glandular elements of the mucous membrane to increased activity will be found of greatest advantage. This can be done best by the administration of the iodides internally and by the local use of stimulating solutions of iodine. These can be advantageously employed in solutions of increasing strength, accompanied by potassium iodide, in glycerin as a medium. Another remedy of service is potassium chlorate, in the form of lozenges, to be dissolved in the mouth at frequent intervals. The patient should use a gargle consisting of hot salt solution, or of some alkaline antiseptic solution at frequent intervals.

RETROPHARYNGEAL ABSCESS

Etiology.—Suppuration in the retropharyngeal tissues is of very common occurrence in young, healthy children. It occurs but rarely in adults, and, in the adult cases reported, the infection has been generally traceable to a pus focus in the immediate neighborhood of the pharynx, such as a spinal abscess or a carious tooth. In children, retropharyngeal abscess frequently follows diphtheria, scarlet fever and measles.

Symptoms.—The onset is insidious, frequently three to six days elapsing before the attention of the physician is directed especially to the throat. For some days before localizing symptoms present themselves, the child will be obviously ill, as shown by fever, general malaise, and loss of appetite. The first symptom directing attention to the throat is generally pain on swallowing. Very shortly the voice becomes muffled, dyspnoea is soon marked and a dry cough begins. Upon examination a smooth rounded swelling can be detected occupying the postpharyngeal wall and extending downward toward the larynx. In some cases the swelling is seen on the lateral walls of the pharynx, and it is in these instances that the pus burrows downward to the greatest extent. Obstruction to respiration may cause marked cyanosis. Erosion of a bloodvessel by the pus is a very dangerous complication. During the past winter the present writer saw one case terminate fatally from this cause and one in

which life was saved by prompt ligation of the external carotid artery. The condition is not, as a rule, accompanied by any very marked fever, generally not above 101° F. In adults, the most prominent symptom is dysphagia, the dyspnœa not being nearly so marked. A very usual accompaniment is cervical adenitis and in many cases abscess formation occurs in the cervical glands requiring incision.

Treatment.—By the time a retropharyngeal abscess has made itself evident as such, the pus has generally pointed to such an extent that its evacuation by incision is urgently indicated. This can readily be accomplished without a general anesthetic if the parts are well cocaineized. Should pointing not have occurred, it is well to make several incisions into the swollen tissues, as this relieves the pain and frequently prevents further accumulation of pus. Applications of ice to the neck externally generally affords relief to the pain. If an early incision is not made the pus is apt to burrow, as a rule, in a downward direction, and very serious results have been reported. Death has occurred from hemorrhage from the carotid or other arteries, and from œdema of the larynx.

LUDWIG'S ANGINA. ANGINA LUDOVICI OR ACUTE PHLEGMONOUS PHARYNGITIS

This is a quite common and frequently fatal purulent infection of the neck which is essentially a deep-seated diffuse suppuration of the sub-mucous pharyngeal tissues, and is due to streptococcus infection.

Symptoms.—The attack, as a rule, begins with a chill, soon followed by intense pain in the throat, difficulty in speaking and swallowing, and sometimes marked dyspnœa. The temperature becomes elevated, sometimes to 104° to 105° F., and the pulse is correspondingly rapid. Examination reveals an intense congestion and swelling of the pharynx, generally bilateral and extending downward, frequently involving the epiglottis and adjacent tissues. The throat externally is swollen; the tissues feel hard and tense to the touch. Difficulty in deglutition develops very early and is soon followed by dyspnœa, with cyanosis. Rapidity of onset and a rapid course are characteristic features.

Treatment.—The disease is characterized by great physical prostration, so that free stimulation is indicated from the onset. Locally, cold should be applied. The swollen pharyngeal tissues should be freely opened wherever a purulent focus can be located. In many of the reported cases, tracheotomy was necessary. If pus can be detected anywhere in the tissues of the neck incision should be made. Death may occur from suppuration, sepsis, or exhaustion.

VINCENT'S ANGINA

An acute or subacute inflammation of the tonsils characterized by the formation of small multiple ulcerations covered by a thick dirty gray exudate, which tends to reform rapidly after cleansing. The membrane and the ulcerated areas contain a fusiform bacillus and the spirillum of Vincent, named after Vincent, who first described the condition in

1898. The ulcerations have a tendency to appear on the mucous membrane of the pharynx and mouth.

Etiology.—It was at one time supposed that Vincent's angina was predisposed to by unhygienic living conditions or depressed vitality, but its very extensive prevalence among the soldiers in the Great War, who were as a class strong, healthy men, leading healthy, open air lives led to a revision of this view. The infection is undoubtedly more frequent in those who have bad teeth and pyorrhœa, and has been traced in some instances apparently to the use of tinned foods.

Pathology.—Although the ulcerations are usually small and multiple, there are cases of undoubted Vincent's angina in which but one large ulcer is found. The exudate presents quite distinctive characteristics. It is closely adherent to the underlying ulcer and the surface of the latter usually bleeds slightly on detachment of the membrane. In order to find the characteristic organisms it is necessary to take a smear directly from the membrane or from the ulcer, as the organisms do not grow on ordinary culture media. Vincent's angina frequently occurs in association with diphtheria or scarlet fever and the diagnosis of its existence is not made because by ordinary culture methods the other organisms are easily demonstrated.

Symptoms.—The characteristic membrane covering the ulcerations is very evident as a rule on inspection. The pain attending the ulcerative process is often very great, sometimes quite disproportionate to the visible evidences of the disease. There is usually some involvement of the cervical lymphatics and occasionally this becomes a preponderating feature. Though suppuration in the cervical glands is not frequent it does occur in quite a number of cases and is always a serious complication. There is not as a rule much pyrexia unless there is glandular involvement. Dysphagia is a marked feature but there is seldom much interference with respiration or phonation except in the fortunately comparatively rare cases which progress to a fatal issue through extension to the larynx and trachea.

Diagnosis.—The condition is sometimes difficult to diagnose on inspection from *diphtheria*, but the characteristic bacteriological findings readily clear up the situation. It has been confused with *syphilis*, and a Wassermann test may be required in order to make absolutely certain.

Treatment.—The removal of the exudate by hydrogen peroxide and forceps or swabs in order to cleanse the throat and permit of the application of antiseptics to the ulcers is the first indication. As antiseptic applications to the throat ulcers many agents have been recommended. Among them are arsenaphenamine, methylene blue and trichloroacetic acid. Personally the writer has found nothing better for this purpose than a strong solution of iodine. Nitrate of silver should be avoided as it coagulates albumen and therefore has a tendency to retain the organisms in a plug of exudate. If one of the strongly corrosive antiseptics is used the surface to which it is to be applied should first be cocaineized. Prompt attention should be given to the condition of the teeth and any that are badly diseased should be removed. Cleansing alkaline throat sprays should be liberally used. The patient's general health should

be maintained and he should be carefully watched until there is absolutely no evidence of any local lesion in order to obviate the danger of a recrudescence.

AGRANULOCYTIC ANGINA

Attention has of late been directed to a curious, and fortunately very rare, form of ulceration of the mucous membrane of the mouth and throat to which the name agranulocytic angina has been given. It was first described by several German observers by whom the name was given. Beatrice Lovett¹ reports a case and gives references to the German literature. The characteristic lesions are rapidly spreading ulcers on the tonsils and pharyngeal walls, frequently also on the gums, larynx, tongue, and genitalia. The patients so far reported have all been middle-aged women, and the disease has invariably terminated fatally within a few days. The most characteristic feature of the disease is the blood count. The hemoglobin and red cells are normal but the white cell count is remarkably low with marked increase in the lymphoid cells. In Dr. Lovett's case the *B. pyocyaneus* was obtained in cultures from the lesions and from the spleen, and the same organism was found in two of the German cases reported. Skiles² reports a case in many respects similar to that reported by Lovett, except that the *B. pyocyaneus* was not found in the cultures and the spirillum of Vincent and fusiform bacilli were present. In Skiles' case icterus was absent. Lovett's case was in a woman, aged forty seven years. Both patients died after a very short illness.

ANGIONEUROTIC ŒDEMA OF THE PHARYNX

This peculiar affection has in recent years been brought prominently to the notice of the profession by the comparatively large number of cases reported. T. H. Halsted³ reported a number of cases and appended a full bibliography. The diagnosis at times presents considerable difficulty. The affection occurs in connection with digestive disturbances, usually in persons of neurotic tendencies. It is frequently seen in association or alternating with attacks of urticaria. As a general rule, the appearance of wheals on the pharynx is accompanied by similar lesions on other parts of the mucous membrane of the upper air passages. Death from rapidly occurring œdema of the larynx has been reported. The symptoms are a feeling of fullness and pain in the throat. On examination, clear, pellucid swellings are seen, varying from the size of a small pea to a cherry, distinctly circumscribed, and without any associated congestion of the mucous membrane. The wheals may remain for some days, or disappear within a few hours.

Treatment.—The effects of local treatment are but slight. We should direct our efforts to finding what lies at fault in the digestive or eliminative systems. Alkalies in large doses have seemed to be of service and the

¹ *Jour. Am. Med. Assn.*, 1924, **83**, 1498.

² *Ibid.*, 1925, **84**, 364 and 1415.

³ *Trans. Am. Lar. Assn.*, 1905.

salicylates have been used. There seems to be in some instances a tendency to spontaneous subsidence of the trouble, cases having been studied in which there was no recurrence after a duration extending over some years.

DISEASES OF THE TONSILS

The faucial tonsils are really a large pair of lymphatic glands, the functions of which are but imperfectly understood. As with other lymph glands, they probably protect the organism from infections of various kinds by acting as filters, and by in some way lessening the toxicity of microorganisms which come within their sphere of activity. Although they are beneficent in their activity, the tonsils are very subject to morbid changes. Thus they frequently become hypertrophied to such an extent as to interfere seriously with normal respiration, and they undoubtedly, under many circumstances, instead of acting as protectors against the invasion of microorganisms, serve rather as portals of entry. The bacterial flora of the tonsillar surface is surprising in its number and variety and many virulent bacteria are found in the crypts.

Morbid changes in the tonsils play a most active part in the etiology of rheumatic fever and of the endocarditis and chorea which are so frequently seen in association. The tonsils as part of the lymphatic system are subject to involvement in the various disorders of it; thus, hypertrophy of the tonsils is most frequently seen accompanying the condition known as the "lymphatic diathesis." There are several factors which render the faucial tonsils especially susceptible to inflammation. Their location subjects them to constant exposure to the inspired air and contact with food or other things which may be taken into the mouth, and their irregular surfaces with wide open cryptic orifices make it an easy matter to understand the frequency with which they become the site of local infections, the source of focal infections.

ACUTE TONSILLITIS

Practically every acute inflammation of the tonsils involves both the parenchyma and the follicles of the gland. It is therefore better to consider acute tonsillitis under one head than attempt to divide the disease into the parenchymatous and follicular varieties.

Etiology.—The chief predisposing cause lies in hypertrophic enlargement of the glands. The exciting cause of the attack is usually found in exposure to cold or damp.

Pathology.—There is congestion of the tonsil with much epithelial proliferation especially manifested in the lining of the follicles. The desquamated epithelial cells, mixed with the fibrinous inflammatory exudate, accumulate within the follicles and appear upon the surface of the swollen tonsils as white patches. Cultures from these white masses show many bacteria, especially staphylococci and streptococci.

Symptoms.—The attack may involve one or both tonsils. It is accompanied by much pain in the throat. This is usually constant in character, and increased by efforts at talking or eating. It frequently extends up toward the Eustachian tube on the affected side. The patient generally experiences great difficulty in phonation. Occasionally the tonsil becomes so swollen as to seriously interfere with swallowing; there is not apt to be any interference with respiration. Accompanying these local symptoms, the patient usually complains of headache and backache. The attack, as a rule, is ushered in by a chill, or at least by chilly sensations; the temperature soon becomes elevated, generally, however, not much higher than 102° or 103° F. The tongue is usually coated and the bowels constipated, and there is almost always marked malaise frequently out of proportion to the objective symptoms.

The cervical glands on the affected side generally become somewhat swollen. Opening the mouth is very painful, sometimes so much so as to give great difficulty in the proper examination of the throat. When the throat is examined one or both tonsils appear swollen, with patches of grayish-white or white exudate filling the crypts. There is also, practically always, more or less redness of the surrounding tissues.

Diagnosis.—As a rule, this presents no especial difficulty. The most serious error is to confuse it with *diphtheria*. In diphtheria, the exudation which is seen upon the face of the tonsil is of the nature of a membrane, which is closely adherent to the underlying surface. Upon attempting to wipe it off, it will be found very firmly attached, and, if wiped off, the underlying surface will bleed; the false membrane is also, as a rule, tinged with blood. The exudate in diphtheria is apt to be found on neighboring structures as well as upon the tonsils; thus, it frequently involves the uvula and the pharynx. A bacteriological examination is to be relied upon for final decision.

Prognosis.—An acute tonsillitis usually subsides in three or four days if promptly and properly treated, but the patient may be left in a very weak and depressed condition. There are practically no sequels, except that frequent attacks seem to increase any hypertrophy of the tonsils already present.

Treatment.—The constitutional management is of as much importance as local treatment. It is wise to give a mercurial purge followed by a laxative salt. In acute tonsillitis the salicylates will be found to exert an almost specific action. The earlier their administration, the more efficient is their action, and they should be pushed to the therapeutic limit. Should there be much fever, one of the coal-tar antipyretics may be combined. Locally, the crypts of the tonsils should be cleansed of the deposits in them by peroxide of hydrogen applied in full strength with a cotton swab. After the application the throat should be sprayed with an alkaline wash, and a solution of nitrate of silver (1 to 8) applied to the inflamed area. This should be done daily, and in the interval the patient should be instructed to gargle his throat every two hours with peroxide of hydrogen diluted about one-half its full strength, afterward gargling with normal salt solution or an alkaline antiseptic solution, and to use a gargle of 1 per cent. acetyl salicylic acid for pain. Frequently

great benefit may be derived from lozenges containing guaiacum, chlorate of potash, or sodium benzoate. The patient will derive much comfort from sucking cracked ice, which not only lessens the pain but also the congestion. Externally, cold applied to the throat is grateful.

PERITONSILLAR ABSCESS OR QUINSY

The term "quinsy" should be confined to suppuration of the peritonsillar tissues and not applied to the occurrence of pus within the structure of the tonsil itself. In most cases there is more or less involvement of the tonsil in the inflammatory process, but in many instances the tonsil is not invaded at all. Quinsy is most frequently seen in persons with large or ragged tonsils, the wide-open cryptic orifices apparently affording a convenient portal for the entrance of the infective micro-organism.

Pathology.—The pus from a peritonsillar abscess may show one or more varieties of staphylococci and streptococci. The abscess generally forms in the loose cellular tissues immediately surrounding the tonsils, and burrows in various directions, especially into the tissues of the soft palate and downward into those of the pharynx. The loose arrangement of the tissues in this neighborhood facilitates the spreading of the pus. The abscess usually points above the tonsil behind the anterior palatal fold. Although quinsy most frequently occurs on but one side, bilateral cases are quite often seen.

Symptoms.—The onset is usually marked by a chill followed by a rapid rise of temperature (103° to 105° F.). From the beginning the patient complains of intense pain in the throat, a pain that is gnawing and throbbing, much aggravated by attempts at eating and talking, and usually extending up in the direction of the ear on the involved side. With this the patient complains of headache; the tongue is furred and the bowels constipated. Articulation is much interfered with, the patient talking as though his mouth were full. There is almost always great prostration.

Diagnosis.—This, as a general rule, presents but little difficulty. Examination reveals the peculiar location and nature of the swelling, and palpation readily elicits fluctuation when pus has formed. A case has been reported in which a physician opened an aneurism, mistaking it for a quinsy. This hardly seems possible with the absence of inflammatory symptoms and if the peculiar pulsation was taken into account. From the sore throats which are associated with the acute exanthemata, the diagnosis should be readily made, considering the location and character of the swelling and the absence of membrane. Tumors or new growths of the tonsils have been confused with it, but in such conditions the acute inflammatory symptoms are wanting.

Prognosis.—Although, as a rule, favorable as regards life, cases with a fatal result have been reported. This generally occurs because of the rupture of the abscess into the air passages, with death by asphyxia, although several cases have been reported in which death occurred from hemorrhage, the result of erosion of a bloodvessel. Each attack is apt

to be followed by recurrences, probably because of some local condition favoring infection.

Treatment.—The salicylates should be given as soon as the attack is recognized, and their use continued until the patient is thoroughly under their influence. Their action is greatly aided if they are given in conjunction with an alkali, such as sodium bicarbonate. Alkalies have also a local beneficial action, and, if the patient uses an alkaline gargle or takes a little sodium bicarbonate into his throat at frequent intervals, it will be found very serviceable. A teaspoonful of the ammoniated tincture of guaiacum in milk every four hours in many instances seems to modify the attack. It is also used in the form of lozenges. The bowels should be opened by the administration of a mercurial, followed by a saline.

Locally, the pain is much relieved by the patient sucking cracked ice. He should also be given a spray or gargle of diluted hydrogen peroxide. This is especially useful after the abscess has been opened, as it burrows into the tissues and gets at the pus in a way nothing else can. The use of cocaine locally to relieve pain is inadvisable, as its constricting effect upon the bloodvessels is followed by a reaction which renders the pain if anything worse than before it was applied. Cold to the neck externally is very grateful. As soon as pointing occurs, the abscess should be opened. The incision should be made under good illumination, the tongue being kept out of the way by a tongue depressor and the parts having been previously cocaineized. The incision should be directed downward and inward toward the median line, in order to avoid opening the large vessels in the neighborhood of the tonsil. After the pus is once evacuated the quinsy generally clears up very rapidly. After the attack is over, the patient should have his throat examined and if the tonsils are diseased they should be removed in order that the dangers of reinfection may be lessened.

CHRONIC DISEASE OF THE FAUCIAL TONSILS

The real functional importance of the tonsils is so little understood that the question of their pathology is obscure. In early life, under normal conditions, they present the ordinary structure of a pair of lymphatic glands. Although their overgrowth or hypertrophy may cause serious interference with respiration, the most important condition which demands their treatment or ablation is when they become the source of infection, either local or general, or when alterations in their structure render them subject to repeated attacks of inflammation with various sequelæ, such as peritonsillar abscess, infection of the lymph glands of the neck, or suppuration of the middle ear. The association of pathological conditions of the tonsils with rheumatic fever, arthritis and endocarditis is proved beyond doubt. The following systemic infections have also been definitely traced to the tonsils in many instances:

Myocarditis, pericarditis, chorea, acute or chronic nephritis, neuritis, sciatica, lumbago, fibrositis, chronic toxemia with debility associated

with anemia, pulmonary abscess, tuberculosis, acne and erythema nodosum.

They are undoubtedly the chief portals of infection in tuberculosis of the cervical lymphatics. The size of the tonsils is no index of their danger as a source of focal infection. Small buried tonsils are much more apt to be foci than large hypertrophied tonsils with open discharging crypts.

Pathology.—As a rule, both tonsils are found diseased, but occasionally the condition is unilateral. Simple hypertrophy is frequent in children and if the tonsil is not otherwise diseased shows a tendency to disappear at puberty. The pathological changes which lead to the development of the so-called "cryptic" tonsils are not clearly understood. The orifices of the tonsils crypts, which are normally closed, present as openings in which accumulations of caseous material containing numerous bacteria are found. This is frequently attributed to repeated attacks of acute follicular tonsillitis. On the other hand, acute follicular tonsillitis is one of the chief manifestations of chronic disease of the tonsils.

Symptoms. Chronic enlargement of the tonsils may exist for many years without giving rise to any notable disturbance either local or general, but usually the patient exhibits at least some degree of the expression characteristic of the habitual mouth breather. Consequent upon mouth breathing is the development of a condition of irritability of the fauces and pharynx, producing a dry, irritative cough. The sleep of children is apt to be restless and disturbed, and, especially if the enlargement of the tonsils is accompanied by the presence of adenoid vegetations in the nasopharynx, nightmare is not infrequent. The voice lacks nasal resonance. If the follicles of the tonsils contain caseous material, the breath is generally offensive. These accumulations, acting very much like foreign bodies, are often the cause of an irritative, non-productive cough, the source of which may be overlooked. Although the patient with chronic disease of the tonsils is subject to repeated attacks of acute tonsillitis, with its sequelæ, it is remarkable how frequently patients with badly diseased tonsils acting as foci of infection will deny having ever suffered from any trouble in their throats. More dangerous than hypertrophied tonsils are the small cryptic buried tonsils from which pus has no exit. The liability to contract diphtheria or scarlet fever is undoubtedly increased by the presence of diseased tonsils. Acute infections of the tonsils may give rise to rheumatic fever, endocarditis, chorea, or nephritis. Cervical adenitis is a frequent complication. The list of chronic systemic infections from diseased tonsils is a long and varied one.

Treatment.—Although many alterative or astringent applications have been extolled with a view to bringing about a reduction of the size of hypertrophied or diseased tonsils, it is doubtful if any of these possess any real value. Iodine is the most useful and is generally used in combination with potassium iodide in glycerin. Glycerol of tannin, nitrate of silver, and sulphate of zinc are rarely used now. Of certain caustics, such as chromic and nitric acid, which were once in vogue, and of the use of the cautery too much cannot be said in reprobation.

If the tonsils are really diseased the only proper treatment unless there are strong contraindications to it, is their *complete removal* by surgical

measures. When the operation first came into vogue it was known as tonsillotomy, a term which fitted very aptly the early method of slicing the tonsil off with a guillotine. Unfortunately this method almost invariably failed to extirpate the entire tonsil and the portion left behind proved as dangerous a focus of infection as the entire tonsil had been. Consequently the guillotine operation fell into disfavor as did another early method, that of attempting to remove the tonsils by means of a punch. Of recent years several modified guillotines, such as those of La Force and Sluder, have been devised, which can be employed so as to completely enucleate the tonsil, in other words perform the operation of tonsillectomy, the only procedure now countenanced for the removal of the faucial tonsils. There are many other methods by which tonsillectomy can be performed. Many laryngologists, after grasping the tonsil with a tenaculum, dissect it from its attachments, and complete the removal with some form of wire snare. Whatever operation is performed perfection of technique on the part of the operator is the chief factor. The operation should, whenever possible, be performed in a hospital. There is a great diversity of opinion as to whether a local or general anesthetic should be preferred. There have been fatalities from both. The point is one which should be decided by the operator with reference to the individual case. Cases of inspiration pneumonia and lung abscess have followed the use of a local anesthetic as well as the use of ether, and the dangers of ether anesthesia have been greatly lessened by the use of the ether vaporizer and suction apparatus which should form part of the equipment of every hospital. The danger of operative infection of the throat is practically eliminated when the operation is done in a hospital, whereas in a private house it is very real. The danger of hemorrhage is ever present in operations on the tonsils. In every large hospital service great numbers of children are sent in by school inspectors and social workers of whose previous history no reliable information is obtainable. The blood coagulation tests are not always to be relied upon either positively or negatively. Hemorrhage can usually be readily controlled by the ordinary surgical methods but when due to hemophilia the serum treatment is the only really practicable method. Cases of death attributable to enlarged thymus, status lymphaticus, have been reported a number of times in association with tonsillectomy. In any case of doubt a preliminary roentgen-ray study of the thorax is a wise precaution.

MYCOSIS OF THE TONSILS AND FAUCES

This is characterized by the presence over the surface of the fauces and tonsils, and in the crypts of the latter, of white masses of granular material and epithelial debris, almost invariably accompanied by the presence of the *Leptothrix buccalis*. In many instances microscopic examination reveals the presence of keratoid material, and many authorities go so far as to consider the process as a keratosis of the epithelium. Others have attributed the condition to the activities of the leptothrix. It is probable that the presence of the latter is more than a coincidence, although it can hardly be regarded as a causal factor, because it occurs

in the buccal secretions of almost all persons, whereas the pathological condition of mycosis is of considerable rarity. There is undoubtedly a marked proliferation of the epithelium underlying the masses, and the latter have an organic relation to the epithelial surface. It would seem that mycotic tonsillitis should be regarded as a proliferative disorder of the epithelial covering of the fauces and tonsils, and that the lesion is frequently of the nature of a keratosis.

The condition occurs in young and otherwise healthy adults; it is very much more common in the female sex. The reason for discrepancy in the sexes is not far to seek, as mycotic tonsillitis is practically never seen in those who use tobacco.

Symptoms.—Definite symptoms are rare. It is usually accidentally discovered during an inspection of the fauces. Occasionally patients complain of slight sticking sensations, especially noticeable during efforts at swallowing, but even this minor discomfort is, as a rule, not complained of by the patient until his attention has been directed to the condition of his throat. Upon inspection the whitish or yellowish-white masses, varying from the size of a pin-head to that of a small pea, are readily seen projecting from the surface of the mucous membrane. The spots vary in number, sometimes only one or two can be found, at other times as many as fifteen or twenty. They may extend down on the posterior wall of the pharynx, and a favorite locality for them is in the glosso-epiglottic space, and about the root of the tongue. The masses stick firmly to the surface, and can be removed only with difficulty, generally leaving a small bleeding spot. Mycosis is unaccompanied by any general manifestations, although its recurrence in association with digestive disorders has given rise to the supposition that there was some relation between them.

Diagnosis.—This presents but little difficulty. Occasionally the masses are mistaken for the accumulations which occur in follicular tonsillitis, and there are cases on record in which a mistaken diagnosis of diphtheria was made. Both of these should be readily excluded by careful examination, and, in case of doubt, a microscopic examination of a portion of one patch makes the diagnosis certain.

Treatment.—The fact that this disease occurs only in non-smokers would suggest that the cultivation of the habit of using tobacco would be an easy solution of the difficulty of treatment. However, in cases in non-smoking men the development of the tobacco habit has not always been efficacious in curing the complaint. So far as local treatment is concerned, the results are unsatisfactory. It is of great importance to attend to the proper hygiene of the mouth and teeth. The patches should be removed as far as possible by frequent application of hydrogen peroxide, nitrate of silver or iodine. In many instances the application of a strong solution of bichloride of mercury is of service.

Much can be done by the removal of the masses by diligent scraping with a sharp curette before the applications of the various solutions. Should all minor measures prove ineffectual, it is frequently possible to effect a cure by the application of chromic acid or trichloroacetic acid, or by the use of the galvanocautery. In many instances the condition continues in spite of all measures and finally spontaneously disappears.

TONSILLOLITHS

The formation of calculi within the tonsils is not very frequent, although it is quite common to find calcareous masses in the caseous material which accumulates so often within the crypts. Tonsil stones are generally the result of calcareous degeneration of the tonsillar secretion which has accumulated in the follicles. They usually give rise to but little disturbance, although the patient may complain of a feeling of fulness in the region of the tonsil in which the stone is located. Their recognition is, as a general rule, easy, although quite frequently they are so deeply situated within the structure of the tonsil that they are only discovered accidentally in a tonsillectomy. The treatment consists in the removal of the calculus by the use of a pair of forceps, accompanied if necessary by the dissection of any tissue which may interfere with its extraction.

CHAPTER III

DISEASES OF THE LARYNX

By H. S. BIRKETT, C.B., M.D.

THE signs seen in and the symptoms referable to the larynx which come under frequent observation fall naturally into two classes. The first of these embraces signs and symptoms in the larynx which betoken or accompany disease of the body elsewhere, such as the change of the larynx in aneurism, tabes, syringomyelia, and others which are particularized below. These are frequently of the greatest diagnostic value, and because they are so diverse do not admit of any more complete classification. The second class consists of inflammatory diseases of the larynx and certain manifestations of a neurotic origin.

LARYNGEAL SIGNS AND SYMPTOMS REFERABLE TO OTHER DISEASES

The importance of an examination of the larynx in many diseases cannot be overestimated, for by means of it a diagnosis which otherwise may be obscure is often made clear at once. It happens frequently that there are no subjective symptoms referred to the larynx, but upon examination very definite signs are found. For example, in an obscure case of aortic aneurism the patient's voice may be absolutely clear, but upon examination a complete paralysis of the left vocal cord is found and the explanation of the absence of any subjective vocal symptoms lies in the fact that the non-paralyzed cord may make such compensatory movement as to definitely approximate the paralyzed cord and bring about the condition essential to clear vocal production. This condition the writer has repeatedly seen when the left vocal cord was paralyzed, due not only to aneurism, but also to other causes producing pressure upon the recurrent laryngeal nerve, such as an enlargement of the left lobe of the thyroid gland and, rarely, enlargement of the left auricle due to mitral stenosis. Too great stress cannot be laid upon the necessity for careful examination of the larynx in all cases of enlargement of the thyroid gland, especially when operative interference is contemplated, as an absence of such knowledge has led to unfortunate results, namely, damage to the non-affected laryngeal nerve.

Paralysis of the recurrent laryngeal nerve may follow *aneurism* of the arch of the aorta, or of the right subclavian artery, or may result from enlarged *bronchial lymph glands*; and from the position the nerves occupy in relation to the *œsophagus*, malignant disease of that organ may produce paralysis of the adductors. In enlargement of either of

the lateral lobes of the *thyroid* gland the recurrent nerve may be involved and produced paralysis of both adductors and abductors. The left recurrent laryngeal nerve is more frequently involved than the right.

In *aneurism* of the arch of the aorta the evidence of its presence is sometimes indicated by distinct pressure upon and visible pulsation of the wall of the trachea. This pressure is in some cases so great as to produce distinct displacement of the trachea, consequent narrowing of the lumen, and accompanying tracheal stridor.

Chronic inflammation of the *apices* of the lungs, such as tuberculous consolidation and chronic indurative pleurisy, may involve the recurrent laryngeal nerve of either side, but more especially the right one.

In *tabes dorsalis*, the abductors, as proved by Semon, are especially liable to be affected. This abductor paresis is often a very early sign; it is usually bilateral, but may be unilateral. In a patient examined by the writer the only sign was a unilateral (left) abductor paralysis, and in the course of a year he showed definite signs of *tabes*.

In *glosso-labio-laryngeal paralysis* and in *syringomyelia*, abductor paralysis is observed. In *typhoid fever* the vocal paralysis presents no characteristic type, the laryngeal muscles being affected either singly or in groups. The writer has seen the abductors involved in one patient. This is the most common type. "The nature of the paralysis is regarded as a peripheral one, but it is still a matter of dispute whether the muscles, themselves, or the peripheral nerves, suffer a pathological alteration" (Friedrich). In chronic *lead poisoning* either the abductors or adductors may be involved. There is no typical form for the paralysis.

Definite *neuritis* of the laryngeal nerve has followed influenza or exposure to cold winds, resulting in paralysis of any of the group of intrinsic muscles.

INFLAMMATORY DISEASES OF THE LARYNX

Acute Catarrhal Laryngitis.—This may occur as a primary affection or secondarily as an extension of a similar condition of the upper respiratory passages.

Etiology.—The most frequent cause is an undue exposure to cold or a damp atmosphere. Other causes are: Excessive use of or improper method of using the voice; direct injury to the laryngeal structures or indirect injuries by foreign bodies, either within or in the neighborhood of the larynx; inhalation of irritating vapors, to which those whose occupation compels them to inhale dust, such as bakers, stone-cutters, etc., are particularly exposed; sedentary habits; living in badly ventilated rooms; alcoholic excesses; swallowing of corrosive liquids. The gouty diathesis also predisposes to it. It may occur in any of the exanthemata, especially measles and smallpox: it may arise also during an attack of influenza or typhoid fever. Defective nasal respiration acts as a direct exciting cause.

Pathology. The changes are similar to those of inflammation of mucous membranes elsewhere. The mucous membrane is hyperemic, swollen, and dry looking, especially over those parts where it is loosely

attached, such as the false cords and the interarytenoidean space. This is accompanied by the active production of cell and mucous elements. Sometimes necrosis of the superficial epithelial layer takes place resulting in slight erosion. This is most frequent on the edges of the true cords about the middle third, and is occasionally seen on the vocal processes and the interarytenoidean space. Œdema may follow.

Symptoms.—In the adult the subjective symptoms are generally very slight. There is a feeling of dryness and irritation of the throat, soon followed by hoarseness, which may increase to complete aphonia. A desire to clear the throat and a dry, tickling cough are present with subsequent expectoration of a small amount of clear mucus, sometimes tinged with blood. Usually there is no febrile disturbance. Objectively, in the very early stage, the true vocal cords lose the normal brightness of their upper surface; later, this condition gives place to the appearance of very fine bloodvessels coursing over the whole length of each vocal cord. In more marked cases this hyperemia becomes uniform, extending frequently into the subglottic region and upward involving the false cords and aryepiglottic folds. At this period of the inflammation the mucous membrane becomes swollen, with the result that the true vocal cords become rounded, especially about the middle third. When the very acute stage has passed the presence of a mucopurulent secretion distributed over the recently inflamed region is to be noted. Upon phonation in the terminal stage of acute laryngitis slight bowing of the vocal cords is seen as the result of a paresis of the internal tensor muscles. In children, owing to the small size of the glottis and the parts about it being less rigid and resistant than in the adult, the disease is apt to produce rather alarming symptoms, such as dyspnoea, which comes on suddenly accompanied sometimes by the pertussis paradoxus. The temperature in children will range from 100° to 102° F., and objectively the whole laryngeal mucous membrane is hyperemic, the bloodvessels on the true cords often being quite distinct. Occasionally, minute hemorrhages are to be seen upon the upper surface of the true vocal cords and in some cases superficial erosions occur on the anterior third of each vocal cord. In children suffering from dyspnoea, who will permit a laryngoscopic examination to be made, the mucous membrane below the glottis is found swollen and bulging toward the middle line (false croup). Children who have enlarged tonsils or adenoids, or both, are liable to recurring attacks of acute laryngitis.

Diagnosis.—In the adult the subjective and objective symptoms are quite clear, but in children a diagnosis is not so readily made. The difficulty of examining the larynx of a child is easily overcome by the use of Jackson's direct laryngoscope. The one condition for which it is apt to be mistaken is *laryngeal diphtheria*. This is generally associated with membrane deposited elsewhere in the upper portion of the respiratory tract, but without the presence of this condition a bacteriological examination of the secretions from the larynx will remove any doubt. The possibility of a foreign body in the larynx being mistaken for acute laryngitis, especially in children, must not be overlooked. The writer saw such a case which had been treated for six weeks for "croup" and

upon examination a piece of chicken-bone was seen to be lodged in the subglottic region.

Prognosis.—This is always good in primary cases, but with any of the infectious diseases a more guarded prognosis must be given.

Treatment.—The patient should remain in a room of an even temperature (65° F.), preferably in bed. Functional rest is most important. Locally, the use of steam inhalations with the compound tincture of benzoin (1 to 10), for five minutes every four hours, is, as a rule, sufficient to relieve most patients. In children the best method of using steam inhalations is by means of a croup kettle. The application of cold to the larynx externally, by means of an ice-bag or ice-coil, is preferred by some. In order to relieve the cough, which often is troublesome, the following will be found beneficial:

R—Menthol	ʒj (gm. 4)
Eucalyptol	ʒij (cc. 8)
Ol. menth. pip.	ʒiij (cc. 12)

Five drops of this should be placed on a respirator and inhaled for twenty minutes every four hours. If there be any febrile disturbance, small doses of tincture of aconite may be given. It is well in most cases to begin with a saline purgative. In children the symptoms of dyspnoea are sometimes relieved by the use of emetics. The application of heat or cold by means of cloths will sometimes relieve an attack. In severe cases when there are signs of respiratory obstruction, intubation is indicated. Enlarged tonsils and adenoids in children who suffer from recurring attacks of acute laryngitis call for surgical interference.

Chronic Laryngitis.—Etiology.—This is usually the result of frequent acute attacks and often of extension of chronic nasal and nasopharyngeal catarrh.

Pathology.—The changes are those of hypertrophy of the mucous membrane, which may be general or local. When affecting the ventricular band, this thickening may be so marked as to hide the true cords; or the changes may be localized to the vocal processes (pachydermia of Virchow), or to the interarytenoidean space. The submucosa is infiltrated with cells and the mucous glands are swollen and distinct.

Symptoms.—Subjectively, the most common symptom is the frequent clearing of the throat in order to remove a huskiness of the voice. In singers the voice loses its timbre and there is a sense of fatigue in the region of the larynx after moderate use. The expectoration is usually tenacious in character, small in amount, and expelled in the form of small pellets of a grayish color.

Objectively, the vocal cords have lost their bright white appearance and vary in color from a pale pink to a bright red and are thickened. This may be limited to the ventricular band, or distinct thickenings may be seen in the interarytenoidean space. Sometimes this hyperplasia of the connective tissue is limited to the subglottic region (chronic subglottic laryngitis). On the surface of the true cords the mucus may be disposed in small pellet-like masses and upon abduction the mucus is drawn into bands stretching across the glottis from one cord to the

other. In long-standing cases there is often a paresis of the adductor muscles and an insufficiency of tension. In public speakers, singers, and teachers, small nodular thickenings, at the junction of the anterior with the middle third of each vocal cord, are occasionally met with. This same condition (nodular thickening) may be found in young boys, due to shouting and improper use of the voice.

Diagnosis.—Usually there is not much difficulty in recognition but, as many patients with pulmonary tuberculosis have chronic laryngitis as one of the early symptoms, it is advisable to examine the lungs and sputum of all patients who do not readily improve under local treatment. Hoarseness occurring in young infants is usually due to the presence of *papillomata* which when of sufficient size will produce very definite, and at times, urgent dyspnoea. Persistent hoarseness in the adult should lead one to suspect a growth, and in an individual beyond middle life is strongly suggestive of *malignancy*.

Prognosis.—As the tendency of most catarrhal affections of the respiratory tract is to return, one cannot give the same hopeful prognosis as in the acute form. In the case of singers and public speakers one must be very guarded.

Treatment.—As chronic laryngitis is frequently a sequence of chronic catarrhal affections of the nose or nasopharynx, it is of primary importance that unhealthy conditions of these regions receive attention. All forms of obstruction to nasal respiration should have careful attention. Where there is an increase of nasal and pharyngeal secretion, a cleansing solution consisting of bicarbonate and baborate of soda, in the proportion of 5 gr. of each to the ounce of warm water, should be used as a spray night and morning. The laryngeal condition should be treated by astringents applied by an atomizer. The following are of considerable value: Chloride of zinc, 15 gr. to the ounce, and argyrol, 40 gr. to the ounce. The application should be made once a day. The use of so-called "dry inhalants" is often of benefit, especially in those patients in whom it is difficult to spray the larynx. Any of the following, either singly or in combination, will prove beneficial: Eucalyptol, oleum pini sylvestris, and terebene; 5 drops should be placed on a respirator and inhaled for twenty minutes three times a day. When paresis of the intrinsic laryngeal muscles exists, improvement is often followed by the local application of the faradic or galvanic current and the administration of strychnine. Absolute rest of the voice is essential and in many persons a faulty method of voice production will require correction. Attention must be given to the general health; change of climate and occupation assist in the more obstinate cases.

Syphilitic Laryngitis.—This may occur in (a) the acquired, or (b) the congenital form.

(a) **Acquired Syphilis.** Primary syphilis of the larynx is extremely rare, only 2 cases having been reported, one by Krishaber in 1877, and the second by Moure in 1890. The lesions are of the secondary and tertiary type, and, concomitantly with these, corresponding cutaneous lesions are frequently found. The period from the primary infection to the development of general infection, as evidenced in the larynx,

varies from eight weeks to three months, but the latter may occur as late as twenty or even thirty years after the primary inoculation. The larynx, from its liability to various forms of catarrhal trouble, is especially apt to show lesions of syphilis on account of the lowered resisting power. From the frequency with which men are exposed, through the variety of occupations of life, to catarrhal conditions of the respiratory passages, they are more liable than women to syphilis of the larynx. There is no relation between the character of either the primary or secondary manifestations and the subsequent tertiary symptoms.

Symptoms.—*Objective.*—The most common lesions of the *secondary* stage are: First, erythema; secondly, superficial ulceration; thirdly, a mucous patch; and fourth, condylomata. Upon laryngoscopic examination the mucous membrane will be found either to be uniformly hyperemic, presenting essentially the same appearance as that of an ordinary acute laryngitis; or it may show an irregularity in the distribution of the inflammatory areas, this being due to interposed areas which are non-vascular, and the whole picture presenting a so-called “mottled” appearance, which, as some authors maintain, is definitely characteristic of secondary syphilis. The areas involved are generally the epiglottis and the false and true cords. This inflammatory process may lead to a destruction of the superficial layer of the mucous membrane, in which case there will be seen a small shallow and irregularly shaped ulcer whose surface is covered with a yellowish colored secretion. The superficial ulcers may extend and unite with others and when healed leave a very thin, stellate-looking cicatrix. The occurrence of the mucous patch within the larynx is comparatively rare. The laryngeal patch is rounded oval, or oblong in outline, of a whitish-gray or yellowish color, and surrounded by an area which is very hyperemic. The localities in which such a patch may be seen are the laryngeal surface of the epiglottis and its edges, the aryteno-epiglottidean fold, the false and true cords. Condylomata in the larynx appear as rounded or oval elevations with a yellowish-colored surface.

Tertiary syphilis manifests itself in three forms: gumma, ulceration, and cicatricial tissue. These conditions exhibit themselves within a period varying from three to twenty or more years after primary infection. The *gumma* presents itself as an infiltration varying in size from that of a very small pea to a size sufficient to produce obstructive symptoms. In appearance the mucous membrane covering it may be of a normal or darker hue, elevated above the surrounding mucous membrane, and its base presenting an area of inflammation of a deep rose color. It may be found on the laryngeal surface and edges of the epiglottis, the aryteno-epiglottidean folds, the interarytenoidean space, the false cords, and the subglottic region. The lesion is usually single but may be multiple. With the progress of time the gumma undergoes a retrograde metamorphosis, as a result of which it becomes yellowish in color, and at last, breaking down, presents the stage of ulceration.

The *ulcer* has generally a circular outline, the edges of which are ragged and thickened, a surface excavated and covered with a dirty yellowish-colored secretion, and a base displaying a zone of hyperemia.

If neglected, the inflammatory process may extend to the deeper-lying structures, and a perichondritis, with subsequent abscess formation, necrosis of the cartilage and its exfoliation, may ensue. Perichondritis may, however, occur without ulceration. It is in this stage of ulceration that dangerous symptoms are apt to supervene. Œdema, either acute or chronic, may arise and produce symptoms of marked dyspnoea, or the exfoliated cartilage may obstruct the respiratory tract; or the loss of the cartilage, especially if it be a portion of the thyroid, cricoid, or arytenoid, may lead to such collapse of the larynx proper as to interfere very materially with respiration. The epiglottis may be involved to such an extent as to interfere with the process of deglutition and allow portions of food to enter the larynx. Fixation of one or both cords, as a result of perichondritis or chondritis, may lead in some cases to a narrowing of the rima glottidis and consequent dyspnoea. Myopathic paralysis of the abductors is not of uncommon occurrence but of very serious moment when present. Finally, hemorrhage may occur and even result fatally, but, fortunately, this happens rarely. A condition described by Fournier as parasymphilitic laryngitis is not uncommon and is characterized by a general fibroid hypertrophy of the mucous membrane of the larynx. It may also be localized to such areas as the false or true cords, or the interarytenoidean space. The chief feature of this pathological condition is its obstinacy to treatment.

The final step is *cicatrizization*. The less extensive cicatrization is evidenced by a white stellate scar of varying extent. The results of ulceration and cicatrization of adjacent structures often lead to the epiglottis being bound down to the base of the tongue or to the posterior or the lateral walls of the pharynx. Bands may be stretched across the lumen of the pharynx and by their contraction lead to great distortion of the structures. Adhesions between the vocal cords may result in web-like bands, which may involve the glottis to a greater or less degree. The cicatricial process may be so severe as to convert the larynx into a mass of cicatricial tissue with a small perforation in the centre acting as the glottis.

Subjective.—In the *secondary* stage they are usually those of a severe, acute laryngitis. The voice is husky or may be aphonic, there is a moderate cough and expectoration of a small amount of tenacious secretion; and, if the epiglottis be involved, deglutition may be painful. In the *tertiary* stage the symptoms are more pronounced; the voice varies from slight huskiness to complete aphonia. Dysphagia is more frequent owing to the involvement of the epiglottis in the inflammatory and destructive processes. Occasionally food finds its way into the larynx when the epiglottis has been considerably destroyed.

It is in the tertiary stage that sudden *œdema* is apt to supervene, and it may produce such grave symptoms of stenosis as to necessitate immediate tracheotomy. When a suppurative process is going on in the larynx there is marked general disturbance, the temperature rising from 101° to 103° F. Externally, the perichondritis or suppurative process may be marked by swelling and tenderness over the affected part; with destruction of the cartilage and its exfoliation there is always danger

of the exfoliated portion obstructing respiration. The breath, when the disease has reached such a stage, is usually very offensive. The expectoration is mucopurulent in character, sometimes tinged with blood, and it may contain fragments of necrotic tissue.

Diagnosis.—The Wassermann reaction is of great value. It is the diffuse laryngitis of the secondary stage that alone requires differentiation from the non-specific acute catarrhal laryngitis. Objectively, there may be at times, and especially when the inflammation is uniformly disposed, considerable difficulty in deciding which of the two conditions is present. The non-specific form of laryngitis yields to the usual methods of treatment, while one should be suspicious of a laryngitis which resists such treatment. A laryngitis in a tuberculous subject may also resist local treatment, but an examination of the general condition and the sputum will materially aid. It is, however, rather in the ulcerative form that difficulties present themselves. The diseases from which syphilis of the larynx requires to be differentiated are tuberculosis and carcinoma. In *tuberculosis* the ulcers are apt to be numerous, the outline not so sharp or distinct, the edges less indurated, the surface not so deeply excavated, and the granulations pale and indolent-looking. The mucous membrane of the soft palate, pharynx, and larynx is pale; there is some febrile disturbance, with increased rate of pulse, and the general appearance of the patient is that of anemia. Smears from the ulcerated areas will often show tubercle bacilli, and an examination of the expectoration will generally give a like result. The two diseases may coëxist and an ulceration originally syphilitic may become tuberculous.

In *carcinoma* the difficulty is greater; here a new growth precedes the stage of ulceration and it is in this latter condition that the difficulty so often arises. In carcinoma the disease presents itself as an ulcerating outgrowth more frequently than as a true, deep, excavating ulcer as in syphilis. The ulcerating outgrowth is more vascular and the surrounding inflammatory area of a deeper color than in syphilis. The progress of a carcinomatous ulcer is much slower than that of a syphilitic one. Other subsidiary points which are frequently considered are: the age, the presence or absence of enlarged glands, and the existence of pain; but these afford very little support to either view.

Microscopic examination of a removed portion is often doubtful in its results, but should be done. In doubtful cases recourse to anti-syphilitic remedies may clear up the difficulty, and yet one must not be too sanguine as to the ultimate results, for iodide of potassium has often the effect of producing absorption of the inflammatory products in carcinoma and thus materially altering the picture. One is sometimes confronted with the further difficulty of syphilis and carcinoma coëxisting.

Prognosis.—This, in any given case of syphilis of the larynx, depends upon, first, the absence of any other coëxisting disease (tuberculosis and carcinoma); second, the extent of the existing lesions, and third, the faithfulness with which the patient will follow treatment. In the secondary lesions, recovery usually takes place without any noticeable changes; in the tertiary stage, when ulceration is present, the progress

is usually readily arrested and the function of the larynx interfered with only so far as the destructive process has extended. When cicatrization has occurred, very little improvement is to be expected.

Treatment.—The effect of arsphenamine or neo-arsphenamine upon all stages of the disease, except cicatrization, is so rapid and so marked that its use is indicated as a preliminary method of treatment to be followed later by mercury and iodide of potassium.

Locally, alkaline sprays, such as Dobell's and Seiler's, and sedative inhalations (compound tincture of benzoin), are indicated, and, after the subsidence of the acute stage, applications of weak solutions (1 to 20) of nitrate of silver. When gunmata or ulcerations are present, iodide of potassium in increasing doses is indicated. Cleansing the ulcerated area with alkaline and antiseptic sprays and the subsequent application of a solution of nitrate of silver, or the insufflation of iodoform will assist. Vegetations may require the use of the curette, forceps, or galvanocautery, to hasten their disappearance. Neither general nor local treatment avails when fibroid changes with extensive hypertrophy have taken place. Adhesion, fibrous bands or membranes, and stenosis of the larynx, require surgical interference.

When syphilis and tuberculosis coëxist it is generally agreed that the syphilis should first receive treatment. In all forms of syphilis of the larynx smoking and the use of alcohol should be prohibited.

(b) **Congenital Syphilis.**—The larynx may be involved at any age, but the disease more commonly shows itself within the first six months after birth. As to sex it is more frequently met with in the female—in the proportion of 3 to 1 (Mackenzie). Three distinct forms are to be met with: In the first, the lesions involve the mucous membrane and the submucosa; in the second, the lesions involve the deeper structures and are characterized by extensive ulceration rapidly involving the cartilaginous frame-work of the larynx; in the third form, there is a deposit of dense fibrous tissue leading to contraction and stenosis.

Symptoms.—In the early stages the symptoms are those of an intense laryngitis, the voice being quite hoarse; nothing more than a very marked hyperemia of all the laryngeal structures is observed. The coëxistence of cutaneous syphilis is frequent. In the second form, the ulceration involving the epiglottis and laryngeal structures is increased and the cry of the child is extremely hoarse and more deeply pitched than in the early stage. The cough is harsh and paroxysmal, leading frequently to an attack of vomiting; deglutition is often difficult. In the third variety the voice is almost aphonic and, as the lumen of larynx and trachea is considerably reduced, there is marked respiratory difficulty which may be accompanied by cyanosis and convulsions.

Diagnosis.—Early forms of the disease may be mistaken for simple laryngitis, but often there are other signs of the congenital form to be seen in the skin and mucous membrane of the mouth and throat. In the more advanced form, the evidence of the disease may be found in the state of the teeth, the condition of the eyes, and cicatrices about the angles of the mouth. The Wassermann test is of great aid.

Prognosis.—This is always grave, but less so in the early stages when, if the affection be recognized and treated, favorable results may be looked for. In the later forms, even when its true nature is recognized, treatment seems to produce less effect than in the acquired form.

Treatment.—Arsphenamine has proved of great benefit, particularly in the ulcerated forms. It should be followed by a course of mercurial inunctions. Pulv. hydrargyri cum creta, gr. $\frac{1}{4}$ or $\frac{1}{2}$ (gm. 0.016 to 0.03), may be given three times a day for several weeks. General tonic treatment should follow.

Tuberculous Laryngitis.—**Etiology.**—The primary cause is the entrance of the tubercle bacillus into the tissues of the larynx. Tuberculous laryngitis may be either *primary* or *secondary*. Primary tuberculous laryngitis is very rare. Secondary tuberculous laryngitis occurs in about 10 per cent. of the cases of pulmonary tuberculosis.

Pathology.—Three stages usually can be recognized: First, hyperemia or anemia of laryngeal structures, associated with an exudate of mucus, pus cells, and desquamated epithelium. Second, a state of infiltration, in which a deposit of minute nodules of diseased tissue, tubercles, takes place most frequently in the interarytenoidean space, vocal cords, epiglottis and in the aryteno-epiglottidean folds, and ventricular bands. The third stage is that of ulceration. The tubercles break down; the ulcerations are at first superficial, but through infection with pyogenic cocci become deeper and more extensive and probably play an important role in the production of perichondritis.

Symptoms.—**Subjective.**—These depend upon the seat and extent of the invasion. If the intralaryngeal structures are involved, the only symptom may be alteration of the voice ranging from light huskiness to aphonia. If the epiglottis or aryteno-epiglottidean folds are involved the chief symptom is dysphagia. Cough may or may not be paroxysmal, and is often preceded by a tickling sensation; there is expectoration of a clear or yellowish-colored mucus—as the laryngeal condition is nearly always associated with pulmonary involvement; shortness of breath is not uncommon; a varying degree of fever (99° to 103° to 104° F.) and a rapid pulse are often present. Functional aphonia (paresis of the adductors or the internal tensors of the cord) associated with general debility, is occasionally met with in early cases of pulmonary tuberculosis.

Objective.—These depend upon the stage in which the disease exists. In the early or *catarrhal* stage the mucous membrane of the larynx may be frequently hyperemic or anemic. If hyperemic there is frequently a marked anemia of the soft palate and pharynx and, what is most peculiar, an extremely irritable state of the throat on laryngoscopic examination. In the stage of *infiltration* the area most frequently involved is the interarytenoidean space. Here the mucous membrane shows distinct thickening, which upon phonation is thrown up into papilliform projections and if the infiltration be sufficiently large it may prevent the approximation of the vocal cords. The surface of the infiltration is often occupied by an ulceration; springing from its base small granulomata may be seen. The vocal cords may present, in addition to an ordinary acute catarrhal state, an infiltration or ulceration. When infiltrated they are swollen,

uneven, and hyperemic. If this be confined to one cord it is strongly suggestive of tuberculosis. *Ulceration*, when present, occurs most frequently on the edges and over the vocal processes. It may be so extensive as to destroy the vocal cords. The mobility of the vocal cords may be impaired, either from extension of the disease into the crico-arytenoid joint or from involvement of the recurrent laryngeal nerve, or some of its branches, by pressure or neuritis.

Next in frequency of involvement is the *epiglottis*, which when uniformly infiltrated assumes a turban shape, and often is sufficiently swollen to prevent a view of the interior of the larynx. It is usually of a red color; the ulcers, which are generally situated on the edge and laryngeal surface of the epiglottis, are deep, and the surface covered with a slough. The aryteno-epiglottidean folds, when involved, are swollen, pyriform in shape, a pale pink or red in color, and the swelling often is so great that they are in contact with the posterior and lateral walls of the pharynx. The ventricular bands may be invaded and swollen; this generally breaks down and leaves a deep ulceration.

Diagnosis.—Laryngeal tuberculosis is generally associated with advanced pulmonary disease, and when such is the case there is usually no difficulty in recognizing the laryngeal lesion. In a small number the pulmonary disease is not easily detected and diagnosis is more difficult. There are some patients who have a slightly irritating cough without expectoration, catarrhal laryngitis, which has resisted all treatment, anemia of the soft palate and larynx, a slight elevation of evening temperature, but no physical signs of tuberculosis. A roentgen-ray examination of the chest may be of some assistance and such patients may be tested with tuberculin. The two diseases which may resemble laryngeal tuberculosis are syphilis and carcinoma. The differential diagnosis is discussed under Syphilitic Laryngitis.

Prognosis.—This “depends on (a) the pulmonary condition; (b) the general reaction; (c) the site of the laryngeal lesion; and (d) its extent and type. As regards (a) and (b) we have also to consider the previous history, the family history any underlying disease (*e. g.*, syphilis or malaria), the age and the mentality of the patient. Other factors are early diagnosis, prompt treatment and after care.”¹

Treatment.—This “must be based on the conception that laryngeal tuberculosis is but a complication of the original infection in the chest.”² The benefit which patients with pulmonary tuberculosis derive from treatment and care in a sanatorium, is frequently reflected in the improvement of the laryngeal condition. Therefore, it is desirable that those patients who can should place themselves under such surroundings.

In the acute catarrhal stage the use of steam inhalation (compound tincture of benzoin, eucalyptol terebene 1 to 150) is beneficial in relieving the cough and moderating the expectoration. A dry inhalant frequently affords considerable relief to an irritating and tickling cough.

The occasional use (once a week) of puncture of infiltrated or ulcerated

¹ Sir St. Clair Thomson: *Tuberculosis of the Larynx*, Privy Council Medical Research Council, 1924.

² *Loc. cit.*

areas by means of the galvanocautery, under the guidance of the laryngeal mirror, has proved to be useful in patients who are afebrile and in good general condition. When the epiglottis and aryepiglottidean folds are infiltrated or ulcerated and dysphagia is marked, this may be relieved by insufflations of small quantities (5 gr.) of orthoform or anesthesine. To obtain relief to the dysphagia by means of a spray of cocaine is not advisable because of the limited time of local anesthesia produced and also from the disastrous effects resulting from its absorption.

When there is *œdema* of either the epiglottis or aryepiglottidean folds, relief is often obtained by puncturing the swollen tissues with a guarded laryngeal knife under the guidance of the laryngeal mirror. Dysphagia due to such conditions is often relieved by injecting 1 cc. of 90 per cent. alcohol into the superior laryngeal nerve at a point where it pierces the thyrohyoidean membrane. Cholier and Bonnet¹ have resected the superior laryngeal nerve for the relief of the dysphagia with very good results.

The treatment of laryngeal tuberculosis by *heliotherapy* has within recent years been sufficiently perfected, and is readily carried out by the patient himself under the guidance of his physician. The method is as follows: "The patient sits with his back to the sun. The sunlight is first reflected from a concave metallic mirror into the mouth of the patient, and upon a metallic laryngeal mirror held in proper position in the throat. A glass mirror is used to view the larynx, for the purpose of observing whether the light is being properly directed. Both the metallic condensing mirror and the glass observation mirror are attached by adjustable joints and supports to a frame which can be conveniently attached to the back of an ordinary chair placed in front of the patient. The patient will usually find it necessary to hold the tongue forward with a gauze handkerchief, and must also have a glass of hot water at hand for heating the laryngeal mirror, exactly as in ordinary laryngoscopic work. After a little practice most patients readily learn to observe their own larynges, and to direct the light upon the lesion. At first very short exposures are made. The time is then gradually increased. Usually at the start an exposure of only thirty seconds daily, gradually increasing to a maximum total of ten minutes, or in a few cases of twenty minutes once or twice a day, was used. At the end of the period of exposure there is observed a certain amount of hyperemia, which disappears in a few hours. No pain is experienced, in fact the method appears to have an analgesic effect on painful lesions. With this method obstinate ulcers heal, infiltrations subside, painful lesions become painless—in fact a steady clearing up and healing of the tuberculous laryngeal lesions. No bad effects from the use of this method have been noted."²

Of still more recent date the application of ultra-violet radiation has given even more promising results.³

In addition to any local treatment, stress should be laid upon the dis-

¹ *La Presse Médicale*, Lyons, November, 9 1912, p. 92.

² C. W. Mills, and A. M. Forster: The Treatment of Laryngeal Tuberculosis by Reflected Condensed Sunlight, *Tr. Nat. Tuberc. Assn.*, 1918, 14, 287.

³ E. Mayer: Theoretical Considerations on the Application of the Ultraviolet Radiation in Tuberculous Laryngitis, *Tr. Nat. Tuberc. Assn.*, 1921, 17, 717.

use of the voice. This point was advocated by St. Clair Thomson in 1901. The use of tobacco and alcohol should be prohibited.

Œdematous Laryngitis.—Œdematous infiltration of the larynx may occur in two forms: (1) *Primary*, which may be subdivided into (a) the non-infectious form—a variety is described by Strubing as an angioneurotic œdema—and (b) the infectious form. (2) *Secondary*.

Etiology.—The non-infectious form is caused by local injuries, the action of corrosive liquids, inhalation of steam, and the internal administration of iodide of potassium, even in small doses. In the angioneurotic form no cause has been found. It occurs in persons of a neurotic temperament and certainly is hereditary, as shown in the series of cases reported by Osler in 1888. Worry, mental excitement, anxiety, and fright are doubtless causes. The writer has seen œdema of the uvula and soft palate follow the administration of an immunizing dose of antitoxin. It is generally associated with œdema of the skin. In the infectious form it is due to the action of pathogenic bacteria.

In the secondary form the causes are those diseases which frequently produce a perichondritis: tuberculosis, syphilis, and carcinoma, typhoid fever, scarlet fever, measles, smallpox, and gonorrhœa (rare). It may also occur in the course of a peritonsillar abscess or an inflammation at the base of the tongue. It may also arise from chronic valvular disease, chronic nephritis, and as a passive congestion from pressure on the veins of the neck.

Pathology.—Œdema of the larynx is characterized by a serous infiltration of the submucous cellular tissue. In the traumatic cases it is usually unilateral, involving the epiglottis and aryteno-epiglottidean folds. In its disposition it differs from the secondary form, which is always bilateral or symmetrical. In the infectious form the infiltration is either seropurulent or purulent. Angioneurotic œdema depends upon an increased irritability of the vasodilator nerves, due either to direct or reflex, central or peripheral disturbance. A spasmodic contraction of the vessels is followed by a paralytic dilatation and stasis or retardation of the circulation; serous exudation ensues, producing acute œdema (Kocher).

Symptoms.—*Subjective.*—The patient usually complains of slight difficulty in swallowing and a feeling of fulness in the throat. The voice becomes husky and, as the œdema increases, it becomes more deeply pitched and inspiration and expiration more difficult and stridulous in character. A distressing and irritating cough is often present. The pain accompanying deglutition often shoots up toward the ears. The swelling of the epiglottis and of the aryteno-epiglottidean folds is often so great that these structures lie in contact with the posterior and lateral walls of the pharynx, and liquids may find their way into the larynx. In the *infectious* form the local condition is generally preceded by a chill or rigor and followed by a rise in temperature (101° to 101° F.). In this form the sequence of events is rapid and prostration most marked, especially in the aged. In *angioneurotic œdema* the symptoms appear suddenly, coming on sometimes during sleep, and may end fatally.

Objective.—Upon examination with the laryngoscope, the epiglottis is swollen and turban-shaped, often so much so as to obstruct the view

of the larynx; the aryteno-epiglottidean folds fill up the pyriform sinuses and the mucous membrane is tense and glistening. The false cords, when involved, are swollen and the color of the mucous membrane of a deeper rose color than that covering the aryteno-epiglottidean folds and epiglottis. Owing to the mucous membrane of the true cords being intimately attached to the cords, there is little swelling, but just below the cords (*i. e.*, infraglottic), where the mucous membrane is loosely attached, the œdema shows itself by distinct swellings.

Prognosis.—This depends upon the cause and extent of the œdema. In the non-infectious cases it is favorable, but in the infectious forms it is most grave. In the secondary form it depends upon the gravity of the primary lesion.

Treatment.—Absolute rest in bed is imperative. The room should be warm and the atmosphere moistened with a steam spray, vaporizing the compound tincture of benzoin (1 to 20). No use of the voice should be allowed. Locally, cold, by means of a coil or ice-bag, should be applied to the neck. The use of small pieces of ice dissolved in the mouth is not advised, as by the time it reaches the involved parts the ice has become nothing more than warm water. A spray of epinephrine (1 to 5000) will often lessen the œdema. Should the obstructive symptoms not abate, the swellings should be punctured by a guarded laryngeal knife, guided by the laryngeal mirror or Jackson's laryngoscope. The throat should be rendered anesthetic by a 10 per cent. solution of cocaine. Pilocarpine, hypodermically (gr. $\frac{1}{16}$ to $\frac{1}{4}$, gm. 0.006 to 0.016) has occasionally proved beneficial.

When the symptoms are not relieved by this treatment, tracheotomy should be performed without further delay. Intubation is not recommended, as the swelling may be so marked as to envelop the opening of the tube when in position.

In angioneurotic œdema, the patients, being highly neurotic, require assurance, and all sources of anxiety and worry should be removed.

Laryngismus Stridulus.—This is a spasmodic contraction of the intrinsic muscles of the larynx leading to closure of the glottis.

Etiology.—*In children* it occurs most frequently between the ages of six months and a year, seldom after seven years of age; it is more common in males than females. These children are usually ill-nourished, badly developed, and often rachitic. Faulty digestion, intestinal parasites, delayed dentition and certain conditions of the pharynx and nasopharynx, such as enlarged tonsils and adenoids, act as causes. In excitable children it may be brought on by violent crying. It is sometimes hereditary.

In adults it may occur as the result of irritation of the trunk of the pneumogastric nerve or its branches, from enlarged bronchial glands, mediastinal growths or aortic aneurism; elongated uvula or enlargement of the lingual tonsils. In locomotor ataxia it may occur, constituting the so-called laryngeal crisis. It may also occur as an hysterical phenomenon.

Symptoms.—In the child the onset is sudden, coming on during sleep, while the child is playing or during crying. The inspirations are short, frequent, and gradually the stridulous character becomes more marked. In a few seconds the short, stridulous breathing gives way to a whistling

inspiration and the attack ceases. The child's face becomes livid, the back and neck are arched, the thumbs flexed upon the palms, the hands on the wrists and the feet flexed and turned inward; consciousness ceases. The spasm may be so severe that the glottis is closed and respiration stops. The face now becomes of an ashy hue and perspiration breaks out on the forehead. The spasm may last from a few seconds to a minute and, when too prolonged, death ensues. The younger the child the more severe is the attack and the more likely to prove fatal. In the adult the attack is similar although much less severe.

Prognosis.—Usually this is good except when the attacks are severe, frequent, or occurring in a very young infant. A rachitic constitution makes the prognosis less favorable.

Treatment.—The condition should be regarded as a local manifestation dependent upon some local or constitutional cause. *During the attack*, the child should be immersed in a hot bath up to its chin; a small quantity of mustard in the bath will act as a diffusible stimulant. Should the spasm be severe, a few whiffs of chloroform often give relief. If the attack is attended with signs of impending death from suffocation, intubation or tracheotomy, preferably the former, should be performed. *In the interval*, attention should be given to correcting any existing general disease, especially rickets. Any gastric or intestinal disorder should be rectified and the child placed in good hygienic surroundings. The administration of general tonics is desirable, especially cod-liver oil; the syrup of the iodide of iron in the strumous subject, and in the rickety child small doses of phosphorus are of great value. In the adult careful examination should be instituted to ascertain the cause and, if possible, rectify it.

CHAPTER IV

DISEASES CHARACTERISTICALLY DUE TO A CONDITION OF HYPERSENSITIVENESS TO SOME FOREIGN SUBSTANCE. HAY FEVER AND ASTHMA

By FRANCIS M. RACKEMANN, M.D.

THE PHENOMENON OF HYPERSENSITIVENESS

Introduction.—The phenomenon of hypersensitiveness manifests itself when individuals who are susceptible to certain foreign substances develop immediately one or more characteristic symptoms when brought into contact with that particular substance. The term "Hypersensitiveness" is long and several shorter words have been suggested, but no one of them is entirely satisfactory. "Allergy" was originally suggested by Pirquet to describe the definite phenomenon of anaphylaxis. It means a "changed reaction." Coca suggests "Atopy," a "strange disease," but the word is still unfamiliar. "Anaphylaxis" applies only to a typical antigen-antibody reaction artificially produced, especially in animals.

The phenomenon of hypersensitiveness is more easily illustrated than defined. The following clinical examples show its importance and indicate that our knowledge of its clinical application, although still far from complete, grows as this application is appreciated.

The most typical example is the man with hay fever whose symptoms occur each year only during late August and September because these symptoms are definitely dependent upon a hypersensitiveness to the pollen of ragweed which is given off into the atmosphere only at this time of year. The city fireman whose asthma is worse when he sleeps in the fire station has horse asthma as shown by his complete relief when motor apparatus replaces the horse-drawn vehicles. The housewife who sneezes only while mixing her dough is hypersensitive to wheat flour. She may also be troubled with asthma and in addition may have eczema on her hands and forearms which clears up to a large extent if she does not touch wheat flour. The case of the man who is so hypersensitive to fish that intense swelling of his tongue and lips results from licking the fish glue from the back of a postage stamp is typical but fortunately rare. If this same man eats fish he may have acute epigastric pain and immediate vomiting or he may have a generalized urticaria; perhaps asthma will occur in addition. The infant who has sudden vomiting when given her first taste of egg-white is clearly hypersensitive to it. Another infant who, watching his mother mix a batter, is hit in the eye with a drop of this batter containing egg-white and is brought to the emergency ward with tremendous swelling of his eye and half his face, shows another manifestation of egg poisoning. An industrial chemist who had asthma which overtook him only after working in the dye labora-

tory of a woollen mill was found hypersensitive to a certain dye. Laboratory workers may sneeze and wheeze when in contact with rabbits and guinea-pigs. Druggists may become sensitive to ipecac, acetanilide, quinine or cocaine, which produce symptoms in the nose or bronchial tree or in the skin.

Sometimes the symptoms are less acute and the relation between them and the causative agent is less clear, but when an eczema of several months standing in a child, is relieved when wheat is excluded from the diet, the hypersensitiveness to wheat is demonstrated. The girl whose chronic sneezing persists from week to week without relation to environment, may be shown to be hypersensitive to her face powder. In these cases, the individual is hypersensitive to some substance, contact with which produces any one of a number of different clinical pictures.

It is important to recognize that the substances to which persons may be hypersensitive include a great variety of agents some of which, as egg-white or wheat, are proteins, while others, as ragweed pollen, certain drugs or dyes, are not proteins and are of relatively simple structure. In normal individuals none of these substances cause symptoms in comparable doses. Whether a substance like poison ivy (*Rhus toxicodendron* or *Rhus venenata*), to which the degree of sensitiveness varies widely, should be included in the same category is debatable.

The symptoms brought on by contact of the hypersensitive individual with the specific substance vary widely. They may be in the nose, in the chest, in the gastro-intestinal tract or in the skin. Such other conditions as migraine, paroxysmal bladder pain, intermittent hydrarthrosis, paroxysmal tachycardia, etc., all of which occur in more or less well-defined attacks may possibly and rarely be dependent upon hypersensitiveness. The possibility indicates the scope of the subject.

The cases cited above have a so-called natural hypersensitiveness. Artificial hypersensitiveness results from the injection of some foreign substance, usually a therapeutic serum. Patients who have been given serum develop "serum disease" and thereafter retain a hypersensitiveness to the particular serum which may be demonstrated in various ways.

Discussion of the whole phenomenon divides itself into various topics.

1. The history of the origin and development of the subject.
2. The immunology of hypersensitiveness and its relation to experimental anaphylaxis and serum disease.
3. The etiology, which is subdivided into,
 - (a) The nature of the "tendency," which renders one person more sensitive than another.
 - (b) The substances to which an individual may become sensitive, grouped according to the mode of contact.
 - (c) The actual mechanism by which sensitization is produced.
4. The diagnosis of hypersensitiveness by the history and by skin tests.
5. The treatment of hypersensitiveness.
6. The clinical manifestations of hypersensitiveness, some of which are characteristic of this condition alone. Included here, however, are hay fever and asthma which are so important clinically that separate sections are devoted to them.

Historical.—In 1873, Blackley recognized that his own hay fever was much aggravated when his daughter placed a vase of grasses in his room. He saw the cloud of pollen which was given off and found that this pollen applied directly to his mucus membranes caused immediate sneezing, and, when an infusion of this pollen was applied to a scratch on his skin, swelling, œdema, and itching occurred promptly at the site. About the same time, urticaria following large therapeutic doses of sheep's blood (serum disease) was described in the literature as due to the treatment, but the true nature of the process was not disclosed until the careful study of Pirquet and Schick in 1905. In the meantime the study of anaphylaxis in animals had begun. Theobald Smith in America and Otto in Germany published almost simultaneously in 1905 their observations that guinea-pigs, having been treated once with serum, often died with violent respiratory disturbances and convulsions when given second doses of the same serum, while normal untreated animals were quite unaffected by much larger doses of this serum.

An observation of great importance was made by Meltzer in 1910. He recognized that the insufflation of the lungs seen in guinea-pigs dead of anaphylactic shock, was quite comparable to the pulmonary distention with emphysema seen in patients with bronchial asthma. This observation made possible some correlation between the phenomena of natural sensitiveness in man and experimental anaphylaxis in guinea-pigs.

In 1912, Schloss described his patient sensitive to eggs, almonds and oatmeal. He did skin tests with various protein constituents of egg-white, of almond and of oat flour, showing that the active substances were protein in nature and also that the blood of the patient contained no antibodies for them. In 1914, Goodale recognized a case of horse asthma by showing that a drop of diphtheria antitoxin placed on the lobe of the ear or on the anterior end of the lower turbinate caused, in each case, an immediate local reaction with swelling, pallor and local irritation. It remained for Walker, Cooke and Vander Veer, and Goodale to develop the subject very rapidly and between 1915 and 1917 to show that not only pollens and horse emanations, but also the dander from dogs and cats and the protein from a variety of foods could cause symptoms in individuals hypersensitive to them.

Immunology.—The small size of the doses and the brief period of contact which suffices to produce symptoms makes it easy to compare hypersensitive individuals with artificially sensitized animals. In many ways the two cases are comparable and hypersensitiveness in man has been erroneously referred to as "Anaphylaxis." But in many other ways they are different. In the guinea-pig, anaphylaxis can be produced only with *true protein substances*. Children and adults can become hypersensitive to true proteins like egg-white or horse dander, but they also can become hypersensitive in an apparently similar manner to various non-protein substances which include not only the plant pollens but also certain coal-tar derivatives, alkaloids, etc., which are quite incapable of producing anaphylaxis in the guinea-pig. The list of these substances is long and is being constantly extended.

Antibodies occur in the anaphylactic guinea-pig and make possible the transfer of sensitiveness from one pig to another. Furthermore the blood serum of an actively sensitized guinea-pig, if brought in contact with the specific serum (antigen), will form with it a definite precipitate. Anaphylaxis is then a true antigen-antibody reaction. From the first, efforts have been made to demonstrate the presence of similar antibodies in human subjects but never with constant results. Cooke and Coca have tried to find precipitins to ragweed pollen extracts in the blood serum of their hay fever patients. Rackemann has searched for antibodies in certain individuals exquisitely hypersensitive to horse dander, and Schloss has tried to find antibodies to egg-white in infants. Occasionally these and similar attempts have been successful but never in a series of cases. In 1919, Ramirez reported the transfer of horse asthma to a healthy man who had been transfused from a donor hypersensitive to horse dander, thus demonstrating the presence of antibodies in this particular donor.

In serum disease in man, the antibody function is better understood. Injections of serum in man are sometimes—and the frequency is greater as the dose is greater—followed, after an interval of about ten days, by “serum disease,” which is usually in the form of a generalized urticaria with some fever and enlargement of the superficial lymph nodes, and is associated with itching. Less commonly it may be in the form of pain and swelling of one or several joints, so that the picture resembles rheumatic fever. Some disturbances of renal function occur at the same time. It runs its course in from one to seven days.

Such a serum disease depends, as Pirquet, Schick and others have shown upon an interaction between the increasing amounts of antibody and the antigen which remains in circulation. As a result of this interaction, a toxic product is formed and the urticaria or joint pains are produced by it. When the serum disease subsides, the antigen (therapeutic serum) can be demonstrated in the blood only in small amounts, while the antibody in the blood serum is plentiful: other antibodies fixed to the cells are easily demonstrated by the local reaction which takes place when a drop of dilute antigen is injected intradermally.

It is important that such a skin test showing fixed antibodies persists for months or years, while the circulating antibodies tend to disappear in weeks. These facts may well have a bearing upon the discrepancies in reports of circulating antibodies in cases of natural sensitiveness.

The principle of desensitization or anti-anaphylaxis is a feature of the guinea-pig experiments. In case a second dose of serum, given to a sensitized guinea-pig, is made small enough, the pig does not die but recovers from his symptoms, and on recovery, can be again injected with the same serum and with large doses of it, but this time without any symptoms whatever.

In human hypersensitiveness, however, the principal of anti-anaphylaxis does not hold. In the course of treatments with extracts of pollen, horse dander, egg-white or other substances to which the patient is hypersensitive, general reactions characterized by marked urticaria, asthma, abdominal pains with nausea and vomiting, or by any combination of these

may occur. In contrast to the experiences with anaphylactic shock, the writer has seen several general reactions of equal severity follow each of three equal doses of ragweed pollen extract given to a patient with hay fever on three successive days. Repeated reactions after injections of horse dander extract have also been observed, so that the theoretical exhaustion of antibodies, as seen in the guinea-pig, does not occur in man, a point of great importance in studying the mechanism.

Multiple sensitization is the rule in human hypersensitiveness and provides one more contrast with anaphylaxis in which the sensitization is always single and very highly specific. A child had eczema which was clearly aggravated by traces of egg and wheat in the diet, and was improved when the diet was changed. This child also had asthma which was relieved only in part by the new diet and was definitely improved only when feather pillows were removed some time after the dietary changes had been instituted. It almost seemed as if the symptoms were due to a summation of causes. In this case, as in many others, the positive skin tests were numerous and were not limited to biologically related substances. In most cases, however, it is hard to prove that other positive tests are of clinical importance and it seems best to regard them with Cooke as "potential" causes of trouble.

Hypersensitiveness to Bacteria.—So far the discussion has dealt with foreign substances readily soluble which when applied to the skin produce a local reaction urticarial in type which appears within fifteen minutes. Skin tests with bacteria resulting in inflammatory areas which appear in twenty-four hours following the intradermal injection of stock as well as of autogenous vaccines have been described. But immediate reactions with pericellular œdema comparable to positive tests with proteins occur infrequently at best.

Such a diagnosis as "bacterial asthma" implies a mechanism at least comparable with that obtained in the typical cases due to a foreign protein susceptibility; and the failure to demonstrate regularly immediate reactions with bacteria or with the products of their growth is disappointing, although study of this subject is far from complete. In the case of bacteria, the active substances are contained within the cells membranes which may be broken down by antibodies in the body without loss of specificity, but in the test tube our methods of extraction are still in preliminary form.

Nevertheless hypersensitiveness to bacteria can be demonstrated and anaphylactic reactions with bacterial products have been produced in treated animals. Hypersensitiveness to the tubercle bacillus is the best known and the tuberculin reaction together with the typhoidin, luetin, mallein reactions, and others have been extensively studied. Here the skin test, inflammatory in type and appearing after twenty-four hours, occurs typically in those cases with a definite focus of active disease (tubercle). More recently, Zinsser has found that the tuberculin reaction can be produced without actual infection when the animal is treated with even relatively small doses—say 1 mg. or less—of dead tubercle bacilli injected three or four times intraperitoneally. In addition to this skin reaction, it has been found possible by Zinsser to sensitize guinea-pigs

with an extract of the tubercle bacillus in such a way that their uteri suspended in Ringer's solution would react specifically when extract is added to the bath, thus producing a reaction entirely analogous to the typical smooth muscle reaction of protein anaphylaxis (Dale, Schultz, Weil, etc.). Thus the ground work for the study of bacterial hypersensitiveness seems established.

Treatment based upon the "positive," inflammatory, twenty-four-hour skin reactions to stock and autogenous vaccines has been advocated but present experience indicates that the effects of such treatment are probably non-specific, that is, are not primarily due to the elaboration of specific antibodies.

Discussion of Immunology.—From this brief exposition of the known facts concerning the immunology of these various related conditions, we can discuss the probable relationship somewhat as follows. When a man receives a large dose of therapeutic serum intravenously any one of three different reactions may result. First, nothing may occur and the serum as injected will disappear gradually from the circulating blood without any symptoms or signs of its presence. If this same man, however, is reinjected at some future time measured in months, perhaps in years, with another dose of the same serum, he is found to be specifically sensitized, a finding which can be demonstrated either by a skin test or by the general reaction which follows immediately when a second dose is given into a vein or under the skin. The amount of the original dose is not of great importance in establishing this artificial hypersensitiveness since we know that guinea-pigs can be sensitized actively with amounts of horse serum as small as one millionth of a cubic centimeter. S. B. Hooker in retesting a group of children with horse serum some months after a Schick test, found evidence of horse sensitiveness in a large number, so that in man it is not essential that the sensitizing dose be a large one. The fact that specific sensitiveness to horse serum can be induced in man together with the fact that such specific sensitiveness is so promptly demonstrated by a second dose of the same serum, makes this experience entirely comparable with the antigen-antibody reaction concerned in experimental anaphylaxis in the guinea-pig.

Secondly, an initial dose of foreign serum may be followed in a proportion of the cases by *serum disease*. The frequency is greater as the original dose is larger. Normally serum disease occurs after an incubation period of about ten days, the delayed (*beschleunigte*) reaction of Pirquet—but it may occur in a shorter time and even come on immediately (*sofortige* reaction), perhaps during the injection. When the serum disease is delayed in the typical manner, the incubation is quite comparable with that necessary in active sensitization of guinea-pigs, which suggests that the initial dose in some way initiates the production of antibody both in cells and serum. In this way it is entirely possible to regard serum disease as identical with anaphylaxis, the chief difference being in the nature of the symptoms, which are produced in man instead of in animals.

The more immediate types of serum disease are, however, related to the third type of reaction. Sometimes the individual is hypersensitive to horse serum and an intravenous dose or even a small subcutaneous

dose may be followed by severe urticaria, asthma and collapse or even death. This rapid and violent reaction is comparable both with the symptoms in the guinea-pig occurring after the intoxicating dose of serum and with those patients with horse asthma or hay fever who are given too large a dose of an extract of the substance to which they are sensitive. The guinea-pig and the patient are both hypersensitive as can easily be demonstrated by appropriate skin tests. The differences between the two have been discussed but it should be emphasized that when proteins are concerned the role of antibodies is apparently definite. On the other hand, exactly the same symptoms may follow an injection of non-protein substances or even slight contact with them, and in those cases antibodies in the blood stream have not been identified, although the presence of a positive skin test would argue strongly for the presence of specific and doubtless protective substances fixed to the cells. Moreover the lack of circulating antibodies may very likely depend upon our inability to identify them if not upon the fact suggested by Zinsser that the function of antibodies is to combine with the antigen in order to promote its removal from the body and that in the case of more diffusible substances such antibodies may not be necessary. It should be noted that in the case of serum disease, circulating antibodies appear early and soon disappear, while fixed antibodies remain indefinitely.

The fact that asthma may be acquired is of fundamental importance, since it is quite easy to conceive that previous exposure to the specific substance has resulted in the production of active sensitization. Nevertheless in many cases it appears clinically that symptoms develop upon the very first exposure and it is apparently impossible to conceive of the way in which previous sensitization was brought about. These are the puzzling cases. The analogy with other cases and the occasional finding that while the dose of egg-white appeared to be the first dose, yet in fact the mother remembers having given the child a piece of cake some weeks previously, perhaps justifies us in overlooking other cases in which such a history of previous sensitization is not easily obtained. The multiplicity of skin tests is another enigma, so far unexplained unless we assume the presence of a group reaction.

There is however one important and perhaps vital difference between true anaphylaxis and human hypersensitiveness, namely the complete and perfect desensitization which follows a sublethal dose in the former while in the latter a dose causing severe symptoms is often not followed by any increased resistance.

In previous observations the interval between the first dose which produced the reaction and the following dose has been as long as twenty-four hours. It is still conceivable that desensitization might develop at once and last for a much shorter period and further experiments may reveal such a finding. The lack of complete desensitization is, thus far, the only insuperable obstacle which prevents us from correlating the facts of anaphylaxis with those of sensitization. The fact that sensitization does not occur among men with much greater frequency depends undoubtedly upon the fact that a "tendency" to become hypersensitive is an important adjunct. Such a "tendency" undoubtedly varies in degree

and may alone explain the irregular occurrence of serum disease. This "tendency" may be a local phenomenon to explain why exposure to horses results in one case in hay fever, in another case in asthma. It is more likely, however, to be a general phenomenon, the local manifestation depending more probably upon the original mode of contact with the sensitizing substance.

Etiology.—Discussion of the causes of hypersensitiveness should deal with the question of why the patient more than his fellow should become hypersensitive. It should deal with the various substances to which an individual may become sensitive and finally with the mechanism by which sensitization is developed. Hypersensitiveness occurs about equally in men and women and in all races. It has been found to develop at all ages from a few weeks old up to sixty years. The common age at which symptoms first appear varies from five years to twenty years. The younger the age at onset the more the likelihood that the symptoms depend upon hypersensitiveness. Nevertheless the writer has seen a man with his first symptoms of ragweed hay fever at the age of sixty. Apparently no age is exempt. The age at onset is important because if it is early, the chance that the hypersensitiveness may be "outgrown" is a definite one. For example, egg poisoning common in young children is rare among adults. Hay fever beginning early tends to disappear after the age of twenty-five years.

The constitution of hypersensitive individuals has been studied in an effort to discover any clinical type characteristically seen with such conditions as eczema, hay fever, and asthma, but with negative results. All three conditions occur in individuals of widely varying types. Blondes are rather more commonly affected than brunettes, but the predominance is not great. Certain types of individuals seem to have one type of asthma more than another but the hypersensitive group of asthmatics is not confined to any one type of individual.

One thinks of some dysfunction of certain glands of internal secretion to explain the tendency to become hypersensitive, but the writer has seen patients with exophthalmic goitre, with elevated pulse and basal metabolic rate, who had attacks of asthma which were quite unrelated to increases and decreases in the degree of thyroid intoxication. Furthermore asthma occurs in myxœdema in which the basal metabolism is considerably below normal.

Suprarenal deficiency, as suggested by the prompt response to epinephrine, is at least not accompanied by the low blood-pressure and the inanition, so characteristic of Addison's disease. Endocrine types, as suggested by obesity, peculiar facial expression, gigantism, infantilism or sexual precocity, are not commonly seen with hypersensitiveness. R. A. Cooke described to the writer a patient with asthma whose attacks occurred regularly at the time of menstruation, which suggested an endocrine-ovarian cause, but this view was exploded by finding the patient very hypersensitive to aspirin which she never took except just before the time of menstruation to relieve the backache which occurred at that time.

More recently Rackemann has suggested that hypersensitiveness could

be acquired and cited a number of striking cases, commenting on the occurrence of industrial asthma to support his contention. The family history in most of his patients was negative and he could observe no clinical characteristics common to the group to explain the tendency to become hypersensitive, except that in each case there was a definite history of prolonged exposure to some particular foreign substance.

Cooke and Vander Veer have shown that hypersensitiveness, as manifested by hay fever or asthma, is inherited according to the Mendelian Law and have found evidences of hypersensitiveness in the families of 48 per cent. of their patients. Other investigators find similar figures. The author found that 60 per cent. of hypersensitive persons suffering from asthma gave a positive family history, while only 10 per cent. of non-sensitive asthmatics gave such a history. So far, inheritance is the only factor found to explain why some individuals become hypersensitive and develop manifestations of it, while others do not. It is possible that overexposure is the only factor, although the relatively low incidence of hypersensitiveness among individuals similarly exposed argues for some other and special reason.

The *mechanism* of sensitization is quite unknown. In young children Schloss and Worthen demonstrated that small amounts of egg-white could pass through the intestinal mucous membrane and be recovered from the blood. It is possible to sensitize a guinea-pig through the respiratory tract and also through the gastro-intestinal tract. Stuart was unable to demonstrate egg-white in the milk of nursing mothers whose infants reacted to egg and could not prove that the hypersensitiveness of the child was acquired in this way, thereby refuting the work of Shannon. From the fact that adult girls sensitive to face powder may use orris root for several years before the development of symptoms, one may conclude that the development of human hypersensitiveness may be a slow and gradual process.

The *substances* to which hypersensitiveness may be developed are best classified according to the means of contact with the individual. Foreign substances may be inhaled or ingested, or the contact may be direct through the unbroken skin or by inoculation. Different routes vary in their importance at different ages. In children, hypersensitiveness to foods is common and the ordinary contact is by ingestion. In adults, however, contact is usually by inhalation and hypersensitiveness to foods is rare.

Inhalation provides the contact with substances in the form of dust. The largest group of dust substances occurs with a definite seasonal relation and is made up of various pollens. When the symptoms are non-seasonal the causes may be in the form of animal dusts, feather pillows, or in a miscellaneous group which includes a wide variety of substances many of which are clearly associated with the home or with the daily work. Here the industrial asthma may be classified. Wheat in the form of flour, orris as face powder, dusts of cotton, wool, leather; certain drugs such as ipecac, cocaine, codeine, etc., and dyes as paramethyldianin, may be included.

It is of considerable importance that many of these substances are

associated with the environment especially the occupation, which suggests that the sensitiveness may be acquired and also makes the diagnosis by the history alone comparatively easy.

Ingestion of various foods to which the child is hypersensitive may result in asthma. Such a contact is rarely seen in adults, but is important in children. Egg-white is the chief offender and it is extraordinary to what degree the hypersensitiveness may show itself since such small amounts of egg-white as are present in cakes or custards may initiate an attack of asthma. Cow's milk is of some importance in certain infants and asthma or perhaps eczema may begin when the baby is weaned.

Next in importance come wheat and other cereal proteins and then a miscellaneous group including a wide variety of foods. The possibilities are practically unlimited although clear-cut cases due to these other foods alone and without a concomitant hypersensitiveness to egg-white, milk or wheat, exist but rarely if at all.

In adults beyond the age of twenty years, foods are the cause of hypersensitiveness in only a very few cases, perhaps not over 5 in 1000, but in these 5 cases the degree of hypersensitiveness is marked. The man so sensitive to fish that he cannot lick a postage stamp without immediate swelling of his lips and tongue has been mentioned. A college student is so hypersensitive to egg-white that any "rich food" must be avoided for fear of immediate symptoms. Smith's patient who could detect buckwheat in the bread on a dining car is characteristic. Food tests in other cases occasionally reveal a positive reaction to one or more foods but the proof that the corresponding substance has any real relation to the symptoms is in most cases difficult, although it is obviously good treatment to completely eliminate such doubtful foods from the dietary.

By *direct absorption* a hypersensitiveness to wheat may be manifested when eczema appears on the hands of a housewife who mixes dough. Drug clerks or dentists may develop a dermatitis upon exposure to some drug. That ivy poison should be considered a manifestation of hypersensitiveness is doubtful because of its wide-spread occurrence, showing that the substance is toxic in itself, the symptoms being produced without the assistance of antibodies.

Subcutaneous inoculation is of theoretical interest only. Attacks of asthma, urticaria or angioneurotic oedema may easily be produced by overdoses of ragweed pollen, horse dander, cat-hair extract, etc., to which the patient is hypersensitive.

Diagnosis of Hypersensitiveness.—The diagnosis of hypersensitiveness is usually easy and it can often be made from the history alone. The *history* is a most important part of the examination and should be taken from the point of view of the detective rather than that of the physician. In many cases the patient is aware of his own hypersensitiveness; he knows that eggs or fish poison him and has learned to avoid them with the greatest care. He may know that he will sneeze or wheeze if he rides behind a horse or if he plays with a cat. In other cases the association of symptoms with particular circumstances should make one suspect a foreign protein cause of trouble and further questions should seek to identify this particular cause. Many miraculous cures which have

appeared to occur when patients were advised to go South or to Arizona might, perhaps, have been brought about more easily by having the patient move to another house thereby avoiding certain dusts or certain beddings which caused trouble at home. The fact that asthma has followed such simple things as going to the theatre or has occurred on nights when company came to dinner suggests such causes as scented soap or a face powder. One man whose asthma occurred only when he went to stay in the country with his grandmother was found hypersensitive to an extract of the dust from the grandmother's farmhouse.

In hay fever the particular pollen, whether from trees, grasses or rag-weed, can be identified by a careful history alone. In cases of multiple sensitiveness the history and perhaps some clinical experiment is necessary to distinguish, for example, between the dog and the cat as factors in the cause of symptoms.

The most important part of the history is that relating to the first attack, which should be studied with great care. In this way a simple pollen asthma as the start of what may have become a chronic bronchitis with emphysema may be recognized. Inquiry as to the occupation often points to some industrial form of asthma and leads to the correct diagnosis. The presence of hypersensitiveness in the family is another point in the history which if positive suggests a hypersensitive cause. Aside from a foreign protein cause, the history will often reveal the association of asthma with such other symptoms as constipation, head colds or menstruation, etc.

Skin tests are of the greatest value in confirming a positive history. Sometimes by themselves they are relatively unimportant although Cooke has described such positive reactions as potential causes of asthma. Skin tests demonstrate antibodies which are fixed to the cells of the skin or to the mucous membranes.

Skin tests may be performed in various ways. First the *scratch method* in which a small quantity of the foreign substance in powder form is mixed with a drop, usually of alkaline salt solution, previously placed on the arm. A scratch is made through the resulting mixture and the reaction is observed after ten to twenty minutes. The positive reactions depend, in the case of foods and dusts, upon the protein content of these powders, which are purified by chemical means and rendered quite soluble. The *intradermal method* consists in injecting between the layers of the skin a small quantity of a solution containing the active principle of the foreign substance in standardized amount. This method is rather more complicated and requires sterile solutions whose nitrogen strength is known and which give no reaction whatever in the skin of normal individuals. With both methods a positive reaction occurs after ten minutes and consists of an urticarial wheal with a pale flat top, sharply-defined borders of irregular outline, and measuring from 8 to 20 mm. in diameter. This urticarial wheal is surrounded by a bright red zone which may be as large as 50 mm. across.

The reading of skin tests is often difficult, especially when the skin is irritable. It is the author's practice to compare the reaction of one substance with that of another and make interpretations only by this

comparison. One test serves as a control for the next. Skin tests with biologically related substances should be placed on the arm as far apart as possible with other tests in between. It would be noted that drugs of the morphine series, especially codeine sulphate, give a positive "skin test" with typical wheal and erythema in most normal individuals, which may be used as a positive control in doubtful cases.

Conjunctival tests are entirely analogous in principle to "skin tests" but are more delicate. A solution of the test-substance is instilled into the conjunctival sac, which if the patient be sensitive, becomes, red, injected and very itchy within a few minutes. If left alone, the reaction will progress until the whole eye becomes swollen. The reaction can be readily controlled by a drop of 1 to 10,000 epinephrine solution or by a drop of 1 per cent. cocaine solution. This test may be used to determine the degree of sensitiveness, as by instilling drops from a series of dilutions beginning with the weakest and adding a stronger drop every ten minutes until a positive reaction is obtained; or it may be used, by virtue of its delicacy, in doubtful cases in which the history of hypersensitiveness is clear-cut but the skin tests by the scratch method and by the intradermal method are negative. A positive conjunctival reaction may confirm an otherwise doubtful diagnosis.

Treatment of Hypersensitiveness.—The treatment of hypersensitiveness is best accomplished by preventing contact with the offending agent. The pedlar with horse asthma who buys a motor car after his horse dies is at once relieved of his trouble. The girl who gives up her face powder stops sneezing and the hay fever victim sensitive to ragweed misses his annual attack if his European sojourn can be prolonged into September. Elimination of the specific protein is the only treatment advisable for young children whose asthma or eczema will clear in a few days if the eggs, wheat, cat, or the feather pillows which singly or together cause trouble, can be removed.

Most asthmatics do well in a hospital, partly because the rest in bed and the care have a good effect, but in many cases, the relief occurs because the substance to which they are hypersensitive and which caused trouble at home is eliminated. Certain enthusiastic authors discuss the importance of "dust-free" hospital wards or rooms and claim that all good results are due to these special surroundings and conditions. Elimination of the offending agent is not always possible and under certain circumstances desensitization is indicated.

"*Desensitization*" with an extract of the offending substance may be undertaken when the symptoms depend upon a hypersensitiveness to some substance, exposure to which cannot be avoided. Such treatment requires a series of subcutaneous inoculations, with an extract of the particular substance, at intervals varying from three to seven days over a period of months. It therefore should not be undertaken without the entire approval and coöperation of the patient. Extracts are made in various ways according to the material. The object is to isolate and dissolve the protein fraction. In the case of cereals, the other substances are removed by dialysis. In the case of animal danders, the oil is washed out by alcohol and ether and the residue extracted with an alkaline salt

solution which is now made with a phosphate mixture to act as a "buffer" and preserve the original degree of alkalinity. Pollens are obtained free of the blossoms and leaves and the pure pollen grains are extracted with similar alkaline salt solution. Alcohol as a 20 per cent. solution in saline is another useful fluid. In each case, the final extract must be *sterilized* by passage through a Berkefeld filter. Standardization is unsatisfactory. Most authors depend simply upon the total nitrogen content of the extract. Although this is known to vary frequently from the biological activity, the method is simple and the results are sufficiently accurate for clinical use.

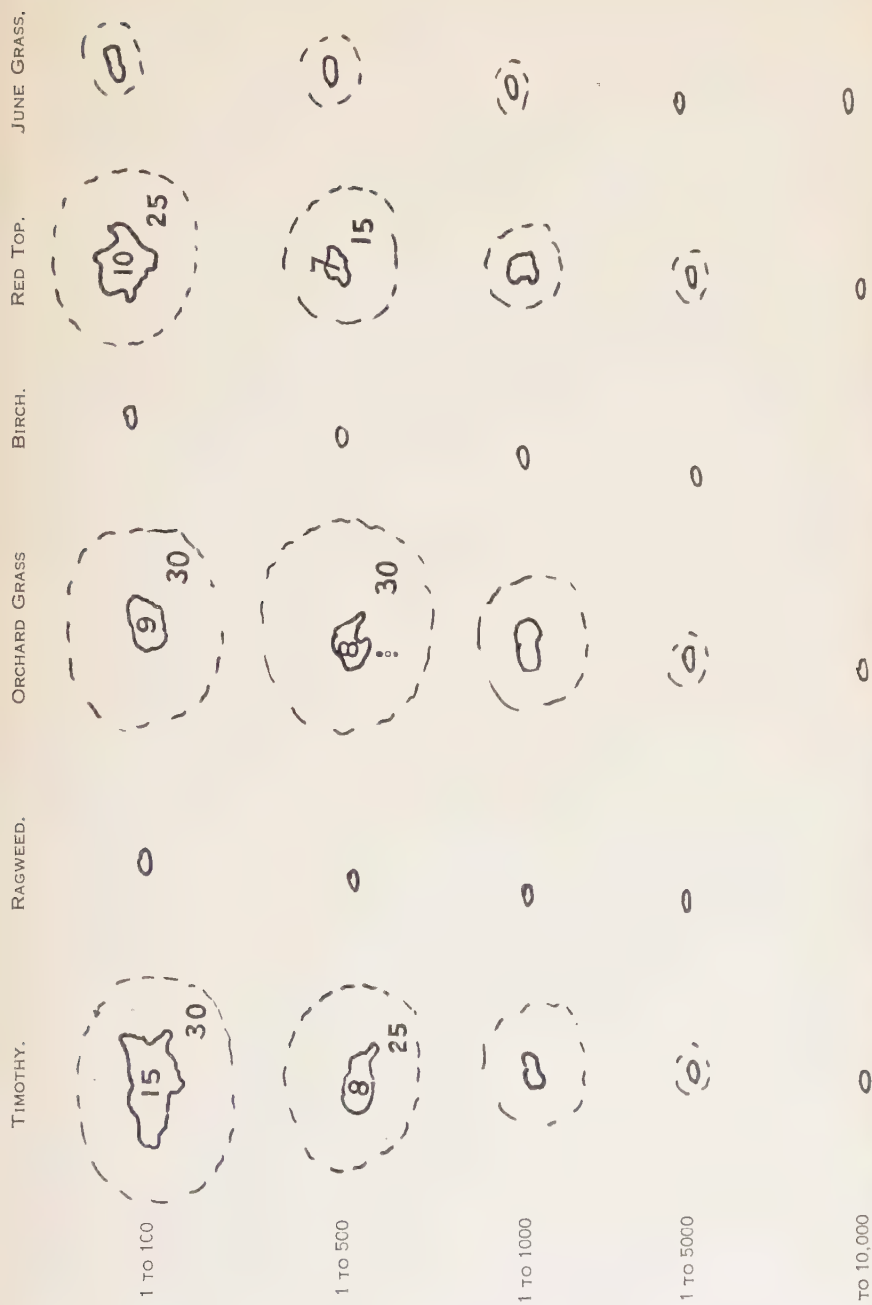
Desensitization is the method now commonly used in the treatment of hay fever. The *procedure* is as follows: The diagnosis of the offending pollen having been confirmed by skin tests, the degree of hypersensitivity may be determined according to a technic suggested by Walker by placing drops from a series of dilutions of the extract on the arm, and making superficial scratches through each drop, beginning with the weakest dilution. The typical local reaction will appear in fifteen minutes at the site of the strongest dilution and of the weaker dilutions according to the degree of hypersensitiveness.

Fig. 6 is a facsimile of the tests obtained in a patient with early hay fever whose symptoms occur only during May and June and who is hypersensitive to several different grasses in about equal degree. Treatment is begun with a small dose (perhaps 0.1 cc.) of that dilution which fails to give a definitely positive skin test—in the case illustrated the first dose was of the 1 to 5000 dilution. Local reactions to subcutaneous therapeutic doses appear within an hour and persist for from six to thirty-six hours as red, swollen itchy areas. The size of the next dose is determined in each case by the size of the local reaction following the previous dose. If the red area was larger than a silver dollar, the previous dose is repeated or perhaps reduced while if the red area was smaller, the next dose can be increased but should rarely if ever be more than double the last dose. The interval between doses should be made shorter if the local reactions are very large. In hay fever, they are ordinarily given at from five to seven days apart.

General reactions may occur during desensitization treatment when doses are increased too rapidly. They may consist of urticaria, asthma or of severe abdominal pain with nausea, vomiting and collapse. Such reactions may come on within a few minutes; ordinarily they can be controlled by a subcutaneous injection of 0.3 cc. to 1 cc. of 1 to 1000 solution of epinephrine but deaths have been reported.

These general reactions are of considerable academic interest since, contrary to our understanding of anaphylaxis, they will recur if the same dose is repeated on the next day. The possibility of producing these general reactions makes the treatment a serious matter, to be undertaken only with all proper caution.

Desensitization treatment is specific in that good results are obtained only in case the extract of the particular substance causing the symptoms is used. For example, in early hay fever in which the patient was apparently hypersensitive to timothy hay, orchard grass and red-top hay,



Tests showing hypersensitiveness to each of three grasses and about equal in degree, with good reactions through the 1 to 1000 dilution of each grass pollen extract. The figures represent the diameter in millimeters of the wheal (inner solid line) and of the areola surrounding it (outer broken line).

treatment one year with timothy failed to relieve, while treatment the next year with red top gave a definite result. A young girl whose asthma occurred only on holidays, when she returned to her father's farm, has been greatly relieved by treatment with cat-hair extract, whereas treatment with horse-hair extract last year failed to help her in spite of the fact that diagnostic skin tests to horse, cat and dog hairs were all of approximately the same size.

The treatment should be continued until large doses have been tolerated with relatively small reactions or until exposure to the offending substance demonstrates a diminution in the hypersensitiveness. Mackenzie has advocated in hay fever the use of an *intranasal spray* of diluted pollen extract for which he claims better results than with subcutaneous treatment alone. The author's experience substantiates this claim, especially in those cases, so extremely sensitive that the dose can be increased from time to time only in slight degree. Theoretically desensitization treatment should bring about a disappearance of the positive skin reaction. In the author's experience however this does not occur, except that the tests with dilutions in series may show a reduction of perhaps 10 per cent. in the degree of hypersensitiveness.

Clinical Manifestations.—The clinical manifestations of hypersensitiveness include primarily asthma and hay fever.

HAY FEVER AND OTHER CONDITIONS

Hay fever, a form of vasomotor rhinitis, is the most typical and most widely studied example of hypersensitiveness. It is an affection of the mucous membrane of the eyes and nose characterized by an œdematous swelling, with nasal obstruction, copious watery nasal discharge and itching of the eyes and nose which are manifestations of hypersensitiveness to the pollen of certain plants. Hay fever occurs only at the season and in the places where the particular pollen is in the atmosphere and can come in contact with the conjunctiva and the nasal mucous membrane. The term hay fever was originally applied by Blackley in 1873 to describe his own symptoms which he showed were caused by the pollen of grasses, but the term is now used to include all cases where pollens of any sort are responsible. "Catarrhus Aestivis" or "Summer Catarrh" was the title under which John Bostock in 1819 described the condition. "Pollenosis" is the modern designation. It is more accurate but less familiar than "Hay Fever." "Rose Cold" is a misnomer.

The symptoms of hay fever are characteristic. The attack often begins with a peculiar itching in the roof of the mouth and a slight sniffing as if a cold was beginning, and in a day or two these symptoms become aggravated. The nose is obstructed, there is intense sneezing, often paroxysmal in character, with a copious nasal discharge which is usually thin and watery. With it there may be more or less conjunctivitis. Some patients have an irritated pharynx due perhaps to the mouth breathing and also a dry hacking cough without sputum. The symptoms are intermittent, may come and go without particular cause, though

changes in weather or environment often bring about a sudden relief of symptoms, or on the other hand, a violent aggravation.

The business man awakes in the country with his eyes red and swollen, and, on getting out of bed, has a paroxysm of sneezing which may continue some minutes. Further sneezing continues until he reaches his office in the city where he is fairly comfortable through the day except for considerable nasal discharge. The trip home through dusty subways or railroad stations starts a fresh attack and through the evening he is quite uncomfortable with frequent paroxysms of sneezing. Sleep is broken and interrupted by nasal obstruction. There is no fever and the degree of malaise is rarely proportional to the local symptoms. When hay fever is severe, it is accompanied by asthma, indeed this complication occurs in about one-third of the cases so that pollen asthma is relatively common.

Etiology.—The seasonal variation in the date of onset and the duration of the disease depend on the production of the particular pollens. In New England the patients are roughly divided into three groups: First, those hypersensitive to the pollen of trees like birch, oak, willow and maple, etc., whose symptoms begin early in May and last only two or three weeks. Second, those hypersensitive to the grasses, the list of which is long and includes chiefly timothy, orchard grass, red top, June grass, rye and foxtail. The symptoms begin early in June and last for about six weeks, until the hay making in early July. The third group is the most important. The symptoms are due to ragweed pollen, and begin in New England in the middle of August and last for six weeks until the frost in late September destroys the plants. This type of hay fever is the most typical and the easiest to study because most of the patients react chiefly to ragweed and not to a variety of different pollens as is the case with early hay fever in which many react to a number of different grasses at the same time, leaving some doubt as to whether the actual cause is one particular grass or several grasses together. Ragweed occurs in several varieties, the two most important being the short ragweed, *Ambrosia artemesiæfolia* and the tall or giant ragweed, *Ambrosia trifida*. The latter is of much more importance in the Southern states than in New England. Scheppegeirell in his book on *Asthma and Hay Fever* gives some excellent photographs and descriptions of different hay fever plants and the pollen given off by them.

Mixed cases, or patients who are susceptible both to grasses and ragweed, are not uncommon. Typically they experience an interval of comparative comfort from the cutting of the hay until the blooming of the ragweed. When this interval is lacking, hypersensitiveness to such pollens as daisy, plantain, clover, etc., must be suspected.

This arrangement of hay fever causes into three groups, characteristic of New England, does not hold for all parts of the world. Thus in the Western United States various grasses, notably rye grass, salt grass and Bermuda grass cause trouble from early May to early July; while in the late summer, sage brush and poverty grass share the responsibility with ragweed.

In England the grasses are abundant and early hay fever is similar

there to the United States but ragweed does not occur either in England or on the continent which explains the fact that during the World War many United States soldiers in the A. E. F. escaped their usual attack of fall hay fever.

The general considerations of age, sex, and race as well as the underlying "tendency" which may be inherited have been discussed in the chapter on Hypersensitiveness and also the mechanism by which sensitization is developed and may be demonstrated.

Treatment.—This consists in the treatment of the underlying hypersensitiveness, the general principles of which have been described. The details need additional comment. The object is to reduce the degree of hypersensitiveness to the particular pollen which causes the trouble. This is done by giving the patient repeated injections of an extract of that pollen, in order presumably to reduce the number of fixed antibodies attached to the body cells.

The ideal treatment is aimed at the prevention of the annual attack and is therefore begun about six weeks before the usual date of the onset of symptoms. At this time the patient is tested not only with various pollen extracts in strong dilution, to confirm his history and to determine to which pollen he is most sensitive, but also by tests of dilutions of that pollen, to determine the *degree* of hypersensitiveness. The principles of these tests have been described in the section on Hypersensitiveness.

When the offending pollen has been identified and the degree of hypersensitiveness to it has been determined, the first therapeutic dose is given subcutaneously and should consist of a small amount (say 0.1 cc.) of that dilution which just fails to produce a positive skin test. For example, let us assume that the patient reacts to ragweed and that he gives a positive test to the 1 to 100 dilution which is large, to the 1 to 500 which is still large; to the 1 to 1000 which is considerably smaller and to the 1 to 5000 dilution which is only a little larger than the control. Treatment in this case should begin with 0.1 cc. of the 1 to 10,000 dilution.

Further doses should be given at intervals of about seven days or more often if the local reactions are large and the tolerance small. The size of each succeeding dose is determined by the amount of local reaction to the last dose. If, for example, the last dose produced a red slightly swollen area in the arm, about the size of a silver dollar, the next dose can be increased say by 50 per cent. If the local reaction was more than this, the next dose should not be increased at all, while if it was small or insignificant, the next dose can be doubled, but should rarely be more than doubled.

The number of doses and the total amount of ragweed injected through the season, will vary widely with the tolerance of the individual patient. Satisfactory results will occur in some patients in whom nothing stronger than the 1 to 1000 dilution is used, but in others doses of the 1 to 100 (strongest) dilution will be necessary. Good results are not always proportional to the amount of treatment and several patients, who, in spite of large doses during the previous years, received only slight benefit, have later been much more comfortable when the treatment was pushed with less vigor. On the other hand, the reverse has also been true, namely

better results have occurred when more doses and a larger total quantity, resulting in larger local reactions, were injected in another year. These results suggest that for each patient an optimal amount of treatment is required.

That the treatment of hay fever is highly specific is shown by the fact that whereas, in one year, treatment with the extract of a certain pollen was unsuccessful, treatment the next year with a different pollen was followed by good results in spite of the fact that skin tests with the two pollen extracts were quite similar.

In case the patient is hypersensitive to several pollens at the same time and in about the same degree (and this is frequently the case in those with early hay fever caused by grasses), the author's practice is to carry on the treatment with each of these pollens simultaneously, but the doses of each extract are given quite separately, in different places in the arm. Records are kept of the local reactions following each dose and the determination of the next dose of one pollen extract is quite independent of that of the others.

When pollen appears in the air and is absorbed by the mucous membranes, this absorption should theoretically maintain the desensitization and make further subcutaneous doses not only unnecessary, but, by leading to excessive absorption, perhaps dangerous. Experience, however, shows that it is worth while to continue injecting pollens until sometime after the usual date of onset to maintain the tolerance reached at the beginning of the season.

When the patient does not present himself until close to or after the onset of his hay fever, it is still possible to help him, especially if relatively small doses are given at short intervals and continued until the symptoms have been controlled. In this seasonal, as opposed to preseasonal treatment, the initial procedure of diagnosis is the same but doses are given at intervals of two or three days instead of five or seven days, and the amount of each is made small without great effort to increase the dosage rapidly and thus produce large local reactions, so running the risk of making the patient worse rather than better.

Throughout the whole course of treatment with pollen extracts, the possibility of producing general reactions should never be forgotten. General reactions occur when the tolerance of the patient has been exceeded by increases in the dose. These general reactions, consisting of urticaria, violent hay fever and usually asthma, appear within ten or fifteen minutes and are alarming to both physician and patient. They can ordinarily be controlled by one or two doses of epinephrine (0.3 to 1 cc. of 1 to 1000 solution injected subcutaneously). Deaths from these general reactions have been reported, which means that the pollen treatment must be undertaken and carried out with the greatest care, since without this care, it is of real danger to the patient.

In addition to this treatment by subcutaneous injections, other methods of desensitization have been described. Intranasal sprays of a solution of the offending pollen advocated by Mackenzie to bring about a local desensitization are often of value, though the mechanism of their action may not depend entirely upon a local exhaustion of antibodies, since

Sewall and Powell have demonstrated that intranasal applications have a "peculiar" effect upon immune processes in general. The patient is given an atomizer containing a dilution of the particular pollen extract and instructed to spray his nose night and morning regularly. The strength of the dilution is determined by the tolerance, the object being to make it as strong as possible without producing sneezing. Ordinarily the strength is only one-tenth of that used for subcutaneous treatment. Frequently the spray and the injections can be used together.

In certain patients presenting themselves after the onset of symptoms, the author has observed that the skin tests alone resulted in considerable temporary benefit. This has suggested the intradermal method of treatment, and in several patients treated during recent years, this method has seemed to produce better results than the subcutaneous route, the doses being regulated according to the same principles. Just why this method should give better results is not yet understood.

The *results* of the specific treatment of hay fever are satisfactory. Although success as measured by actual percentages varies somewhat in the reports, yet the variation is not great. It may be said in general that successful results are obtained in at least 75 per cent. of the cases. Absolute cures, in which all symptoms of coryza are abolished, occur in not over 15 per cent. of the total. The results from treatment are not permanent and desensitization must be carried out during successive years, usually with increasing success and with a decreasing number of doses.

Symptomatic treatment is usually unsatisfactory. Oily sprays containing menthol, watery sprays with cocaine and epinephrine, washes, douches and ointments have all been applied to the eyes and the nose, sometimes with temporary relief. In case the symptoms cannot be controlled, the patient must move to a region free of the particular pollen. Grasses grow everywhere and a sea trip is rarely worth while since this early hay fever is usually not as severe as the late form. Ragweed does not thrive at an altitude over 6000 feet. The pine woods of Northern Michigan and Northern Wisconsin are free areas, also the western slope of the White Mountains, including the towns of Bethlehem, Bretton Woods and Dixville Notch, which do not have ragweed and have an elevation of 4000 to 5000 feet. The Moosehead Lake region of Maine is said to be a good locality for hay fever sufferers.

Non-seasonal Vasomotor Rhinitis.—Hay fever is the important group among the large number of individuals who suffer from vasomotor rhinitis. Other patients whose symptoms are quite the same except for the definite seasonal relation, may be found hypersensitive to some substance in the form of dust but not a pollen, while others with negative skin tests are evidently not sensitive and owe their trouble to some intrinsic cause which may be some abnormality in the nose or throat.

In the first group are those hypersensitive to the dust of animals, as horses, dogs, and cats and whose symptoms for some reason are confined to the nose. Feather pillows are occasionally the cause of trouble. The group is a small one for the reason that while many positive skin tests to animals and feathers have been obtained, in only a few of these cases

has it been possible to establish by the history or by clinical experiment, a causative relation between the corresponding animal and the symptoms.

Girls and young women hypersensitive to face powder form a more important subgroup since the elimination of face powder will often cure at once. In a few cases the dust of wheat flour or of some occupational dust, as in a cotton mill, shoe factory, woollen mill, or candy shop, can be identified as the offending substance. In many cases however, a positive skin test appears to be of little clinical importance and such tests must be regarded, as Cooke suggests, as "potential" causes of trouble.

The second group is larger and includes many patients whose histories do not suggest any foreign protein cause and whose skin tests are entirely negative. Here the chronicity and severity of the symptoms may be very distressing and many of these individuals continue for weeks and months with almost constant nasal obstruction necessitating mouth-breathing, and with paroxysms of violent sneezing accompanied by a profuse watery nasal discharge. The members of this group are very difficult to treat. Some intranasal pathology has been suspected and a deviated septum, a chronic infection in one or other sinus, or foci of infection in teeth have been identified and treated but with success in only a few instances. Repeated cauterization of the lower turbinates has occasionally furnished relief which in a few cases has been permanent. The results in general are unsatisfactory.

Vaccines have been used in many of these cases but with only few good results, in spite of the fact that the vaccines were autogenous. The theory of a chronic bacterial infection of the mucous membrane hardly seems adequate.

More recently attention has been paid to other parts of the body and to the general condition of the patient. Correction of eye strain has cured one case: the relief of chronic constipation another, and the institution of proper habits of eating, rest, and exercise has greatly improved a number of these individuals. A cool tub bath in the early morning has resulted in a paroxysm of sneezing but if persisted in, has eventually led to an improvement in the general tone and indirectly relieved the local symptoms to a definite degree. An attack of vasomotor rhinitis is frequently a precursor of an attack of asthma and it is surprising that many patients with chronic and severe vasomotor symptoms do not develop a swelling of the bronchial mucosa comparable to the pale boggy swelling of the nasal mucous membrane so typical of all forms of vasomotor rhinitis, especially when we know that at least one-third of the patients with pollen hay fever develop a wheeze of varying degree and duration during the pollen season. Our understanding of the condition is slight.

Urticaria, Angioneurotic Oedema, Eczema. Like asthma and hay fever, urticaria, angioneurotic oedema and eczema may in certain cases be manifestations of hypersensitiveness.

Urticaria may be acute or chronic. The acute attack with generalized eruption of elevated wheals varying in size from that of a split pea to a silver dollar, may occur suddenly and last for a few hours to a few days. Such an outbreak may be associated with slight fever and usually with

some general malaise. It may properly be regarded as due to the formation of some toxic substance.

Certain individuals have urticaria after eating such foods as strawberries and various kinds of shellfish. Urticaria may be produced at once if an individual hypersensitive to some foreign substance, as ragweed, pollen extract or horse-dander extract, is injected subcutaneously with an overdose of that substance. Furthermore, urticaria is the typical symptom of serum disease which appears on the tenth day after large parenteral doses of foreign serum. In other cases urticaria can be traced to a general systemic disturbance, usually in the gastro-intestinal tract, which has occurred from one to two weeks previously, the interval being quite analogous to the incubation period of serum disease. These examples illustrate the fact that acute urticaria may often be regarded as due to some toxic substance.

Chronic urticaria is a more difficult subject as the lesions may come and go in various parts of the body, each persisting for hours or days and the whole disease may last for many weeks. Such cases are very stubborn and resistant to all forms of treatment.

Urticaria from the habitual use of phenolphthalein has been reported and the possibility of hypersensitiveness to any drug being manifested in this way must be borne in mind. Perhaps of greater interest is the fact that such a slight disturbance as occurs after rapid eating of ordinary food may result in urticaria. In spite of a considerable number of observations similar to these, the exact manner in which urticaria is produced remains unknown.

Treatment.—The treatment of urticaria from the point of view of sensitiveness consists in the elimination of those substances which cause trouble and this advice is sufficient for the acute cases due to specific food poisoning, but the number benefited in this way is small. Most patients with urticaria who have been tested with various food proteins, and have taken a diet limited to the foods giving negative tests, have given results usually disappointing.

The treatment of the chronic form is likewise unsatisfactory. Most of the patients cannot be proved to be hypersensitive to a particular substance, nor can the cause of the trouble be often identified. Removal of foci of infection is advised in all cases when they are present, but such removal does not often provide a cure. Vaccine treatment has been used and the author has observed several cases in which the production of fever and chill following the intravenous administration of typhoid vaccine has resulted in an apparently permanent cure. The theory of such treatment is entirely speculative.

Angioneurotic Œdema (Quincke's Disease).—Angioneurotic œdema (Quincke's disease) is closely allied to urticaria. It is characterized by œdematous swellings which occur in various parts of the body, especially in the extremities, under circumstances similar to those of urticaria. Angioneurotic œdema is less common than urticaria, and while it may occur alone and without urticaria, yet the two conditions usually occur together. The demonstration of a definite hypersensitiveness as a cause for angioneurotic œdema is no more common than in urticaria and a study

from this point of view is rather unsatisfactory, but nevertheless the possibility that the condition may depend upon a specific hypersensitiveness must always be kept in mind.

Eczema.—The problem of eczema is beyond the scope of this section but it is appropriate to call attention to the fact that in many cases in children a hypersensitiveness to some particular food may be demonstrated by skin tests and that such a hypersensitiveness can be confirmed by the fact that the eczema clears as soon as the corresponding food is eliminated from the dietary.

This fact applies not only to children on a general diet but also to infants who are still exclusively breast fed, since, in a few of these cases, it has been found that skin tests on the child reveal a reaction, perhaps to eggs or to wheat, and that if the corresponding food (eggs or wheat) is eliminated from the mother's dietary, the eczema in the infant disappears.

O'Keefe finds that 61 per cent. of breast-fed infants with eczema show a positive cutaneous reaction to food proteins and that an apparent cure occurs in about 40 per cent. when the food in the mother's diet is omitted or limited. In none of his cases did the mother show any positive skin reactions to these same foods.

The mechanism by which these infants become hypersensitive is not clear in spite of the fact that certain observations are of considerable importance. Schloss and Worthen demonstrated that even in normal children ingested egg-white can be absorbed unchanged by the intestinal mucosa and later demonstrated in the blood serum. Shannon has sensitized guinea-pigs to egg-white with the breast milk of mothers whose infants were sensitive to egg, thus showing the presence of egg in the milk, but Stuart using the uterine strip method for demonstrating the sensitiveness of guinea-pigs was unable to demonstrate egg in breast milk so that the mechanism is still in doubt.

Skin tests to food substances in adults suffering from eczema have given results in only a very small proportion of the cases. The fact that a dermatitis may occur following contact with the specific substance in individuals hypersensitive to it, as in housewives with wheat flour, dentists with cocaine or workers in certain industries using dyes or other chemicals, has been mentioned.

ASTHMA

Definition.—The term "asthma" by derivation means a gasping. It is used to indicate a peculiar type of dyspnœa which is characterized by difficult inspiration, expiration or both, and which is accompanied by an audible "wheeze," all apparently due to an obstruction to the flow of air in and out of the lungs. This obstruction in turn depends upon a spasm of the bronchial muscles or an œdema of the bronchial mucous membrane, or on both. Asthma occurs in a variety of conditions so that it should be regarded only as a symptom and not as a disease entity. Because of the manifold causes, the diagnosis of "asthma" should, if

possible, be qualified in such terms as pollen asthma, horse asthma, food asthma, bacterial asthma, etc., to indicate the underlying etiological factor. "Bronchial asthma" is a term which is commonly applied to the symptoms of those patients who have asthma either steadily or in definite attacks but who have no other apparent disease. "Spasmodic asthma" indicates that there are well-defined attacks.

History.—In 1698, John Floyer published his *Treatise of the Asthma*, in which he gives a vivid description of his own symptoms which depended upon a "straitness, compression or constriction of the bronchi" and tells how his "fits" were related to the weather, to his diet, to certain odors and to his passions. Until comparatively recently asthma has been considered to be essentially a neurosis. What fundamental knowledge we have of its cause has been obtained only in the past ten years. Meltzer's comparison of asthma in man with anaphylaxis in the guinea-pig was made in 1910. Schloss' description of the child whose asthma was due to eggs was published in 1912 and Goodale recognized the nature of horse asthma in 1914.

Physiology of Asthma.—The difficulty with which air is forced in and out of the chest in asthma depends upon a narrowing of the lumen of the bronchi due to a constriction of the circular muscle fibres or to a swelling of the bronchial mucous membrane or perhaps to both factors. Brodie and Dixon, and later Einthoven, showed that stimulation of the vagus nerve could cause bronchial constriction. Certain poisons like muscarin and pilocarpine could produce a tonic constrictor spasm in the presence of which vagus stimulation caused not additional constriction but an inhibition of the spasm. This was interpreted as showing the presence of two sets of fibres in the vagus nerve, one of which supplied the circular constricting muscles, the other, the longitudinal dilator muscles of the bronchial wall. Preliminary treatment with atropine can prevent the effects of vagus stimulation. Largely because of the striking results following nerve stimulation, and also because they were unable to find in the bronchial mucous membrane any erectile tissue comparable to that found in the nose, Brodie and Dixon concluded that a spasm of the bronchial muscles was the underlying mechanism of asthma, and was much more important than the conception of a swelling of the bronchial mucous membrane as suggested by Clarke or of the "Bronchiolitis exudativa" of Curschmann. Studies on the action of epinephrine in asthma have stimulated further researches. Eppinger and Hess class bronchial asthma with these conditions dependent upon an overactivity of the vagus nerve "vago-tonia." Epinephrine is the typical stimulant of the sympathetic nervous system and its good effect in asthma is said by Eppinger and Hess to be due to its action on the broncho-dilator muscles which are innervated by the sympathetic. Park and Janeway showed that on excised artery rings, epinephrine acted in inverse ratio to the degree of tonus. If the artery was contracted, epinephrine would relax it, while if the artery was relaxed, epinephrine would make it contract. In this way the conception of the sympathetic factor was to them unnecessary and two sets of fibres in the vagus nerve were sufficient to explain the observations. This subject is of considerable importance because of the good result reported by the

Germans as following section of the sympathetic nerve for asthma, which will undoubtedly stimulate further research.

Bronchial constriction causes the symptoms of asthma but it has other effects. Tracings of the respiratory movements taken by S. G. Mudd show a marked prolongation of the expiratory phase, with disappearance of the normal interval between expiration and inspiration. This is due to the fact that normally, expiration depends upon the recoil of the elastic tissue, as well as of the thorax, and is entirely passive. Active expiration results in a positive intrathoracic pressure with compression of the lung and further constriction of the bronchi and consequently takes longer. This mechanism and the relatively greater ease of inspiration explain the development of emphysema with asthma. In contrast to the constriction of the larger bronchi, the terminal bronchioles and the alveoli are dilated, the bloodvessels in the alveolar walls are squeezed and rupture of the wall with initial hemorrhage and ultimate coalescence of adjacent alveoli may occur. These explain the marked and characteristic increase of the pulmonary dead space, with an increase of the residual air which easily accounts for the great diminution of the vital capacity. They explain also the added burden on the right side of the heart, the tendency to hemoptysis, and the low blood-pressure. Cyanosis does not occur in simple asthma without infection, but does occur in infected cases, presumably because the exudate interferes with the proper oxygenation of the blood.

Epinephrine injected subcutaneously affords prompt relief. Its injection is followed by a definite shortening of the expiratory phase, an increase in the volume per breath, in the total ventilation and in the vital capacity. It causes a relaxation of the bronchial spasm and allows free passage of air out as well as in.

Pathology.—As indicated above there are two main theories regarding the production of asthma. The fact that the attack comes on rapidly and may pass off rapidly, sometimes without treatment, but more often following a subcutaneous dose of epinephrine, suggests a true nerve muscle spasm. But the symptoms of hay fever occurring in the nose, where there are no muscle fibres, may likewise begin suddenly and pass off suddenly, following treatment with epinephrine or cocaine solution. The theory of bronchial swelling with exudation is not without some basis. Comparatively little is known about the pathology of asthma because deaths are rare and reported autopsies are few.

Huber and Koessler collected 15 cases from the literature and described the pathological findings in 6 cases observed by them. Their technique was most thorough, in that sections from different parts of the bronchi and adjacent lung were taken in series, from the bifurcation of the trachea to the periphery. These sections showed a certain parallelism between the clinical picture and the structural changes. When the patient had a bacterial type of asthma with abundant sputum the striking lesion was a hypertrophy of the mucous gland system. In other cases with less cough and in which spasm was the predominant symptom, the chief changes were hypertrophy of the smooth muscle system and atrophy of the mucous glands. As might be expected, however, the pathology was

not always clear-cut and most of their cases showed a very definite thickening of the bronchial wall and a variable amount of activity in the mucous glands. This bronchial thickening involved all layers from the epithelium to the outer fibrocartilaginous layer. The authors conclude that "In man, at least, the allergic reaction of the tissues is not confined alone to the smooth muscle fibre system but involves also the whole organ system which serves exudative processes, endothelium, epithelium, capillaries and glands." Incidentally and quite in keeping with the physical findings, the amount of thickening and degree of activity of the gland structures were found to vary considerably in different parts of the lung. Another feature was the presence of eosinophile cells in the bronchial walls; such eosinophiles often exude into the bronchial lumen and are found in the sputum. Their significance is unknown except that they are characteristic of asthma in general. That eosinophiles are of comparatively little value in diagnosis is shown by the fact that they may be abundant in the sputum or in the blood in patients whose asthma depends upon a hypersensitiveness to some foreign substance (extrinsic asthma) as well as in those whose asthma depends upon some abnormality within their own bodies (intrinsic asthma). Furthermore in the blood stream eosinophiles are some times found in increased numbers during the attack and some times in increased numbers in the interval between attacks. A relation between the sputum, eosinophiles, and Charcot-Leyden crystals has been considered but with little fundamental knowledge. In sputa containing many eosinophiles, Charcot-Leyden crystals are said to form on standing.

Etiology.—Asthma occurs at all ages and may begin at infancy or not appear until late in life. It occurs among all races and among all classes of people. The causes are manifold. They are at once divided into *extrinsic* and *intrinsic* causes. The first group is referred to in the literature as the "allergic," "atopic," "hypersensitive" or "foreign protein" group, while the intrinsic causes are designated "non-allergic," "anatomic," "bacterial," etc., or even as Cooke suggests "undiagnosed." The importance of these two groups varies according to age. In children most of the cases are of extrinsic origin but in persons beyond the age of forty years, extrinsic causes are few in number and the majority depend upon some intrinsic cause. The percentage of hypersensitive patients among the adults asthmatics varies according to the method of study and with the interpretation of skin tests. Thus Walker, using the scratch method of testing, finds approximately 40 per cent. in the extrinsic group. Rackemann finds only 31 per cent., whereas Cooke, using the intradermal method which is more delicate, claims that as high as 73 per cent. belong in the extrinsic group.

The *extrinsic* causes may be subdivided according to the method of contact, which may be by inhalation, by ingestion, directly through the unbroken skin, or by inoculation. For discussion of this group, the reader is referred to the section on the Phenomenon of Hypersensitiveness.

The *intrinsic* causes fall into at least two groups, according as they occur in the bronchial tree or in some other part of the body, including the upper respiratory tract. To take the latter group first; infectious processes occurring as various foci of chronic bacterial activity may often

be shown to be true causes of asthma. The removal of abscessed teeth brings about a cure in a certain small proportion of cases. The drainage of an infected antrum or of infected ethmoid cells, sphenoid cells, or frontal sinuses, causes a cure in a certain proportion of cases. It brings relief to most patients for a certain time measured usually in months. The literature on the relation of the nose and throat to asthma is voluminous. Some point to the fact that a large proportion (25 per cent.) of all cases of asthma seen in a large clinic had previously been operated on without any improvement. Others maintain that every patient with asthma has something wrong in the nose or throat and that relief from the asthma is in direct proportion to the care and thoroughness with which the local nasal and paranasal disease is treated. There is no doubt of the importance of the relation between the nose and throat and asthma, and every patient with asthma should have the nose, sinuses and teeth examined. In the author's opinion operations should be done only with very positive findings and then only after other treatment has been unsuccessful.

Many patients whose asthma has been intermittent, perhaps occurring with colds, develop a chronic form of trouble which may later be relieved when it is found that an antrum, for example, previously in good condition is full of pus. The removal of nasal polypi often brings relief, which may last for months or years, but such polypi tend to reappear unless the cause of their formation, usually a chronic sinusitis, is treated. In children with negative skin tests asthmatic bronchitis, occurring either in attacks or steadily, is often relieved and may be cured when infected tonsils or adenoids are removed. Tonsillectomy in adults has been done in many cases but not with success commensurate to the results following the treatment of intranasal disease.

Indigestion is more often a result than a cause of asthma. The treatment of constipation or visceroptosis occasionally brings about a cure of asthma, especially in older women. The author has seen a case of gall-bladder disease, similar to the one reported by Babcock, in which removal of the stones has been followed by freedom from asthma since the operation two years ago. Pelvic disease in women and genito-urinary disease in men should be kept in mind although no case in which asthma was cured by treatment of these local processes has been reported.

The *metabolic* group is definite but small. A few patients have asthma and diabetes at the same time. Study of their symptoms has revealed a definite relation between the asthma and the hyperglycemia. Syphilis and asthma coëxist occasionally and the relation between the two seems definite in a few cases.

Hyperthyroidism and *hypothyroidism* bear little if any relation to asthma which occurs in those with myxœdema as it does in Graves' disease, in which the asthma is unrelated to the basal metabolism. All these cases are in the intrinsic group.

Tuberculosis used to be considered very important in asthma. The diagnosis can be made only in a few cases and usually by the roentgen-ray. In one case the asthma was worse when the fever was higher. The absence of asthma among the patients in tuberculosis sanatoriums is noteworthy.

Bacterial asthma is a term which must still be used without accurate definition. It applies to those cases in which the cause is supposed to lie in an actual bronchitis. In many cases the asthma begins after an acute respiratory infection, perhaps influenza or pneumonia, and since the onset, attacks occur without relation to season or environment but follow a cold or exposure. In other cases no severe infection precedes the asthma which occurs in attacks at long intervals, some of which follow head colds and occur characteristically in the fall and the spring, each attack lasting from seven to ten days. It is important to note that such attacks occur without change in environment, occupation or diet so that the assumption of a foreign protein cause hardly seems reasonable. Similar cases begin to have asthma with the cold weather of autumn and the trouble is prone to continue with variations until spring. "Winter asthma" is an artificial but appropriate designation of still another group. The diagnosis of bacterial asthma in any form is made chiefly by exclusion, because the actual relations of bacteria and their products of growth to the production of asthma has not been accurately defined.

Secondary Infections.—Regardless of the primary cause of asthma secondary infections are prone to occur and mixed causes are therefore common. The patient who begins at the age of eighteen years to have ragweed hay fever, and who several years later develops his first asthma as a complication of this hay fever, has trouble only during the pollen season and is well when the frost comes. But sooner or later he is almost sure to find that this simple "pollen asthma" does not cease abruptly with the first frost but continues into October or even November. This latter asthma is typically associated with cough and sputum which is thicker and more abundant than the tenacious mucus of the simple asthma. It is entirely reasonable to assume a secondary infection to explain such a continuance of the symptoms. Later on, this patient may develop other attacks of asthma, perhaps in the winter and spring, and as time goes on each attack becomes longer and the intervals shorter, until finally, between fifty and sixty years of age, he is harassed by a chronic cough and dyspnoea on slight exertion and has a barrel-shaped chest and cyanosis. At this time his attacks are not defined but he is always short of breath. Such a patient has chronic bronchitis and emphysema but the whole condition has resulted because of secondary bacterial infections which superimposed the mselves on a simple and clearly defined pollen asthma. In the same way secondary infections develop in other forms of simple asthma.

Attacks of asthma from almost any cause are prone to vary with changes in climate, season, or environment. Pollen asthma occurs only in summer. A certain type of bacterial asthma might well be called "winter asthma." Certain patients seem to be better and worse according to changes in temperature, humidity, and barometric pressure, but no reaction with these outside factors common to all cases has been demonstrated.

Certain bodily functions influence asthma, as mentioned under the toxic group. Attacks are apt to be worse at the time of *menstruation*. Constipation has been mentioned. Mental and physical strains resulting in "fatigue" or "nervousness" are of undoubted importance. The diagnosis of nervous asthma should be made only with greatest care, since too

often a true cause of trouble, which was susceptible to successful treatment, has been found in those who at first seemed only "nervous." One patient with "nervous asthma" has had no asthma since the gall stones which gave no symptoms until a sudden severe attack, were removed. Nevertheless the story of the artificial rose producing hay fever is doubtless true and instances of severe asthma occurring with some emotional excitement are common. The writer has occasionally been able to treat asthma successfully with no other means than simple regulation of the daily hygiene, with special attention to regularity of eating, rest and exercise, combined with proper supervision of the dietary, to make sure that the food is simple, easily digestible and suited to the needs of the patient.

Symptoms.—The symptoms of asthma are typical. The picture of the young adult sitting in a chair, leaning forward with his elbows on a table perhaps holding his forehead so that every accessory muscle of respiration may aid to get his breath in and to get it out again, is extreme but not uncommon. He may be found standing up or sitting cross-legged in bed. Cough is unimportant and the scanty sputum is stringy and tenacious. He can talk only with difficulty. In such a patient the subcutaneous administration of epinephrine (Mvii to xv, 0.5 to 1 cc., of a 1 to 1000 solution) will bring about a sudden change within five minutes, the first sign of which is talking. Such an attack is typical. Some patients may have one or two such attacks varying in severity each night. There may be no pain or a sense of pressure or squeezing from the sternum in front to the interscapular space behind.

Examination of the lungs during the attack shows a loud percussion note but the breathing is diminished and high pitched and is usually masked by rales of all kinds, mostly dry and squeaky, which make the typical "music-box" chest. When such an attack passes off the patient is essentially well, though for the next few days he has some dyspnoea on exertion.

Although it is perhaps true of asthma more than any other disease, that no two cases are quite alike, yet the study of a considerable series reveals certain *fairly definite clinical types of cases*. At least five of these are seen with sufficient frequency to warrant special mention.

First is the child between the ages of five and twelve years whose asthma occurs in well-defined attacks, each of which lasts for several weeks and during which the wheezy dyspnoea is severe and the cough distressing. Between attacks the child, although comparatively well and cheerful, is thin and delicate. He has considerable cyanosis and may have some deformity of his chest, either the pigeon breast or a barrel shape. Between attacks emphysema is definite and although there is no complaint of dyspnoea, the breathing is short and often with an audible wheeze. Such a child may be found sensitive to some foreign substance but in most cases no definite cause is apparent and a chronic bronchial infection is assumed, especially where the cough and cyanosis are marked. The tonsils and adenoids are frequently hypertrophied in these children and their removal occasionally cures the asthma. Enlargement of the bronchial glands as demonstrated by the roentgen-ray is a frequent finding.

The *second* form is the young adult with a very definite extrinsic asthma which occurs only under some special circumstance. Very likely he knows that proximity to horses or dogs, or some dust causes his symptoms or he may give a definite story of pollen sensitiveness which explains the seasonal variation. Such a person is apt to be thin but not markedly so and if seen between attacks the diagnosis of asthma cannot be made except by the history. Some members of this group can take part in competitive athletics provided they are able to avoid completely the cause of symptoms during the period of training.

Group *three* may be illustrated by the thin worn, haggard individual of middle age whose appearance suggests tuberculosis but his face is not flushed, he has no fever and he is bright and cheerful. His asthma is severe, coming on with some regularity once or twice each night and yet he is able to carry on his work in spite of his loss of sleep. Cough is not important and the scanty sputum is composed of thin stringy mucus. His chest is somewhat rounded, the breath sounds being everywhere diminished in loudness and high pitched in quality. There are many squeaky rales which come and go depending on the degree of asthma at the time of examination. A characteristic feature is the definite nasal quality of the voice, which gives the impression of recent recovery from a head cold in which the sinuses are still full of secretion. This is the group in which examination of the nose and throat is of the utmost importance. Many of the patients have had nasal polypi removed and nearly all have had one or more operations on the nose and throat. Examination usually shows nasal polypi and the roentgen-ray shows changes of one or several sinuses. Some of these patients can be relieved at least and perhaps cured by adequate treatment.

The *fourth* group is of a different character, as the patient likewise of middle age, is usually well nourished. Cough is much more important. The chest is definitely barrel shaped; the rales are often moist and consonating. The sputum is typically purulent and occasionally bloody when an alveolar wall is ruptured. Cyanosis is the rule and clubbing of the fingers occurs in long-standing cases. Such patients are much worse in the winter months and are more comfortable during the warm weather. Their symptoms are of long standing, ten to twenty years, and the disease appears to make little progress. Some patients in this group give positive skin tests so that it may be possible to trace the origin of their disease to an original primary asthma of the extrinsic type which began many years before. Foci in the nose and throat are not commonly seen in this group. The heart action is good; the blood-pressure about normal; blood eosinophilia may be present but is not characteristic. The bacteria in the sputum vary. During exacerbations, one particular organism may become predominant such as a Type III pneumococcus, the influenza bacillus or a streptococcus. Treatment with vaccines should be tried in all these cases since it may do good in some. Potassium iodide is the one drug of greatest value, the effects of which are often gratifying. Creosote and ipecac may be used.

The *fifth* group is small but in the author's experience is so typical as to warrant comment. In a series of over 1000 cases of asthma followed

with considerable care, the 5 deaths have all occurred in women between the ages of forty-five and fifty-five whose asthma began between the ages of twenty-five and thirty-five years. The history in each case was of asthma which at first occurred only in isolated attacks at fairly long intervals. Later the attacks became worse both as to severity and frequency, until finally they were separated by a few days only and each attack lasted for two or three weeks. In each case the patient had been well nourished, even somewhat fat, and when seen between attacks appeared quite well. The chief complaint has invariably been asthma, while cough has been distinctly secondary and the sputum rarely thick and purulent. Skin tests have either been negative or the positive reactions have not been related to any particular circumstance which would justify the explanation of a definite cause. Examination of the nasal sinuses has revealed disease, and in each case a nasal operation had been performed. The pulse remains rapid between the attacks but regular and without cardiac enlargement or signs suggesting heart disease. Each of these 5 patients had been moved from one environment to another, usually to a hospital where in spite of clean, dust-free surroundings and adequate care the asthma did not improve. In fact at times the severity of the attacks became so great as to justify the administration of chloroform or ether when large doses of morphine, atropine, and even hyoscyne failed to give relief. Epinephrine, which had relieved during the early stages, invariably lost its effect toward the end in spite of large doses given every hour. In each case death occurred suddenly after a severe spasm which came on without apparent cause and lasted continuously for over twenty-four hours. In the 1 case in which an autopsy was made there was extreme pulmonary emphysema and a dilatation of the right ventricle with thinning of its wall but no other lesion in heart, lungs, large bloodvessels or other organs. Tentatively the cause of the asthma in these cases has been considered to be outside of the respiratory tract, the bronchial constriction being reflex in nature.

Other Symptoms and Signs.—*The sputum* varies with the amount of bronchial infection from a thin watery clear tenacious mucus showing only a few eosinophile cells and on culture only a few organisms, mostly streptococci, to a thick greenish-yellow purulent sputum which appears at the end of the attack. More typically in cases with definite chronic bronchitis the sputum shows eosinophile cells and a profuse growth of organisms many of which are staphylococci, and frequently pneumococci or influenza bacilli.

The blood picture is fairly constant. The leukocytes range from 8000 to 12,000 and eosinophiles may be present. The fact that the percentage of eosinophiles may be high or may be low, either in extrinsic cases or in intrinsic cases, or that it may be high or low during attacks, or between attacks, indicates that the percentage of eosinophile cells is not of particular importance in diagnosis.

Cyanosis is found only in the infected cases and varies with the extent and degree of infection. The cyanosis depends upon an oxygen-unsaturation of the blood due to the exudate in the bronchi which interferes with the normal exchange of gases.

A disturbance in the *acid-base relationship* has been demonstrated by Scott in cases of emphysema associated with chronic asthma of some standing. Whereas normally the respiration responds, as shown by Peabody, with a characteristic rising curve in the amount of ventilation per minute, Scott found a very different reaction in emphysema. As the carbon dioxide is increased the respiratory response is greatly lessened until finally a definite "break" occurs and quite suddenly the ventilation increases and the dyspnoea becomes severe and distressing. This peculiar reaction is explained by Scott as due to the presence in the blood of a relatively large amount of available alkali (bicarbonate) which is able to combine with much more than the usual amount of carbon dioxide without change in the blood reaction. The "break" is easily explained by the fact that even this excess of alkali is eventually used up so that dyspnoea occurs with suddenness and severity.

The vital capacity is diminished in all cases, due to the markedly enlarged dead space. *The blood-pressure* is typically low and one feature is the striking fall of the systolic pressure during inspiration; indeed the sucking effect of inspiration may make it difficult to obtain the systolic pressure at all. *The kidney function* is normal even in the extrinsic cases which is interesting in view of Longcope's finding that repeated doses of foreign protein may cause an interstitial nephritis in animals.

The roentgen-rays studies are important. In early and uninfected cases during or shortly after an attack the lung fields are clear and bright; the ribs are spread apart; the diaphragm is low and its dome flat, its angle with the chest is more obtuse than normal. Under the fluoroscope its excursion is seen to be limited. Peribronchial thickening is a common finding and discrete lymph nodes may be identified. The extension and degree of this peribronchial thickening vary. It may spread upward toward the apices suggesting an old tuberculous process or it may be spread practically throughout the lung fields giving a picture of pulmonary fibrosis which appears to be characteristic of a certain type of chronic infected asthma. It is worth noting that asthma is not common in Hodgkin's disease although in a few cases the disappearance of asthma following roentgen-ray treatment was almost as marked as the change in the chest plates. All of this suggests that in these cases asthma is caused not so much by large masses of glands which press upon the trachea and bronchi as it is upon one particular gland which by its location sets up a chronic nerve irritation.

Course.—This varies widely according to the cause and type of the disease. Emphasis should be placed upon the fact that in adults, asthma tends to progress from a relatively simple uncomplicated result of hypersensitiveness to an advanced secondary infection of the bronchi leading ultimately to myocardial strain and damage. On this account it is of great importance to recognize the cause and institute proper treatment at the earliest possible date. Asthma which begins in childhood tends to disappear after maturity.

Treatment.—**Treatment of the Attack.**—Epinephrine is the one valuable drug in asthma. The prompt injection subcutaneously of 0.5 cc. of the 1 to 1000 solution should relieve the attack within five minutes. The dose

is important. Too much epinephrine produces muscular tremor, pallor, and headache, while too small a dose will not relieve the asthma. The proper dose relieves the attack without producing the unpleasant symptoms. Sometimes as little as 0.2 cc. is as effectual as a much larger dose although there are cases in which 0.7 cc. had no effect, but 1 cc. gave prompt relief. Epinephrine stimulates the broncho-dilator nerve fibres, particularly their endings in the bronchial muscle. Atropine in doses of gr. $\frac{1}{100}$ to $\frac{1}{50}$ (0.00065 to 0.00032 gm.) may be tried. It paralyzes the endings of the vagus and theoretically should end the attack by cutting off the stimulus. Practically, it is far less effective than epinephrine. One writer has distinguished between the causes of asthma acting in a reflex manner through the vagus nerve, whose effects can be cut off by atropine and those which act locally on the bronchial mucous membrane and are controlled only by epinephrine, which of course controls the first group also.

Other therapeutic measures include the use of "asthma powder" of which there are numerous proprietary brands on the market. These powders, pastilles or cigarettes contain mixtures of powdered stramonium leaves and saltpetre. A small amount of this powder when placed in a saucer and lighted, gives off a dense smoke which can be inhaled and gives definite relief. To many patients the use of a "pet remedy" of this kind is quite indispensable. Mild attacks of asthma are often relieved by this alone. In using such a powder it is unnecessary that the entire room be filled with smoke. Better results can be obtained by using a paper cylinder so that the fumes pass in more concentrated form from the saucer to the patient's face. Hot steam from a saucepan of boiling water often relieves an attack. The addition of compound tincture of benzoin (a teaspoonful to the quart) to the hot water is useful especially if cough is marked. Allied to these simpler measures are the intranasal sprays of cocaine or epinephrine solution which are highly treasured by some patients. The fact that these sprays applied to the nose can relieve symptoms in the chest speaks strongly in favor of a nerve reflex originating in the nose as a cause of asthma in these patients.

The air in the patient's room should be fresh but warm as cold air almost always aggravates the condition. The patient should be kept warm especially if he must sit in a chair. Placing the feet in hot water is often helpful. The application of poultices, plasters or an electric pad to the chest has been advocated and is worth a trial. The best treatment for an acute attack is, however, prompt removal to a hospital; the object is three-fold: The change of environment may remove the patient from some dust which causes trouble at home, Second, proper care under good conditions improves the bronchitis and epinephrine can be given promptly whenever necessary; and finally, facilities for determining the cause of asthma are at hand.

Preventive Treatment. — Preventive treatment has three objects. If the patient can be proved hypersensitive, the particular substance can be avoided or desensitization can be carried out as described in another section. But if he is not sensitive the first object is to remove all foci of infection. While bad teeth are extracted, sinuses explored and drained,

and tonsils removed in many cases without ultimate improvement, yet we have at present no way of telling in advance whether a proved focus of infection will be important or not and consequently it is the practice of the writer to advise removal of any focus which can be clearly demonstrated.

A *roentgen-ray study* of the chest should be made as a routine. A large thymus in children may cause a "thymic asthma" but rapidly improves on roentgen-ray exposure. Enlargement of the bronchial glands in patients of any age is a common finding. Roentgen-ray treatment is worth trying, especially in older patients with definite hilus shadows, although at this writing, the procedure is still in the experimental stage. Two patients, whose asthma was severe enough to require 8 or 10 doses of epinephrine in twenty-four hours, have been treated with fairly heavy exposures of the roentgen-ray over both sides of the chest, front and back (four exposures in all) and both of these patients have been almost freed of their symptoms, perhaps because of the effect on the hilus glands.

Finally, when foreign substances can be excluded, when foci have been removed and when the roentgen-rays fail to show any definite hilus glands, vaccines may be tried.

Vaccines have been used widely and with varying results. They may be made from the patients own organisms, which are isolated each in a pure culture, or they may be made from stock cultures. In 1923 the writer published a report of the results of vaccine treatment in which it was brought out that good results depended entirely upon the fact that the vaccine produced a definite local reaction at the site of inoculation. This general conclusion applied with equal force whether the vaccine was autogenous or stock. Further experiences have confirmed this observation and at present the procedure is to isolate those organisms which are most common in the sputum, each in a pure culture and from each culture to make a vaccine. Small doses of each vaccine are then injected subcutaneously (the intradermal method has been found too delicate and to give results which are confusing when the skin is very irritable). In twenty-four hours the local reactions, inflammatory in type, are observed and usually are found to vary in that one of the several vaccines produces a local reaction larger than the others. With this particular reaction-producing vaccine treatments are carried out at intervals of five to seven days; each dose being regulated by the local reaction following the last treatment. Sometimes only one vaccine is isolated and its local reaction is then compared with subcutaneous doses of stock vaccines. When stock vaccines have produced good local reactions, the results of treatment with them have been as good as with autogenous vaccines. Recently W. S. Thomas has reported analogous results but with autogenous vaccines only.

The author's experience with these different vaccines leads to the conclusion that the treatment is non-specific. Mackenzie has obtained good results with ordinary typhoid vaccine.

Non-specific Treatment.—Treatment which is deliberately non-specific has included injections of defibrinated blood, which in certain cases have produced good results. Injections of milk have been used. Auld in England advocates the injection of peptone solution. The keynote of

success in the treatment of asthma lies in the ability to appreciate that the causes of asthma are of many different kinds, each of which includes many individual varieties and then to discover and treat the underlying cause of the symptoms in the particular case under observation.

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CHAPTER V

DISEASES OF THE BRONCHI

BY ALEXANDER MCPHEDRAN, M.D., LL.D.

ACUTE BRONCHITIS

Introduction.—Owing to the exposed position of the air passages to the outer air with its impurities, bronchitis is the most common disease of the respiratory organs. The protective agencies of the upper air passages consist in the filtering of the air of its coarser substances by vibrissæ of the anterior nares; then as it passes through the nasal cavities, the pharynx and the larynx, many of the foreign particles and bacteria are abstracted by the mucus, a process that continues in the trachea and large bronchi whose highly vascular mucous membrane freely secretes mucus rich in phagocytes. The air in passing through such a tortuous course is warmed and can rarely fail to be largely if not completely cleansed of organisms and foreign matter. The cough excited by the sensitiveness of the mucous membrane of the trachea and large bronchi affords further opportunity for the absorption of deleterious matter by the mucus as well as its expulsion from the respiratory tract. These conditions account for the fact that in the majority of cases the disease affects only the trachea and larger bronchi. For these reasons, the air entering the lobules of the lung is probably generally free from organisms and foreign material.

The usual division into *acute* and *chronic* is useful, and, in general, correct, although there is no definite line of demarcation, the one gradually merging into the other; yet the distinction between the two is well marked. In *chronic bronchitis* there are definite connective-tissue changes in the bronchi, or a constitutional state lowering vitality and rendering such changes liable to occur, so that infection, although important, plays only a secondary part in its causation; while in *acute bronchitis*, on the other hand, *infection* plays the chief role.

Etiology.—In many cases, chill from exposure to cold, especially if the air contains much moisture, is the primary exciting cause of bronchitis. The chill causes spasm of the arteries of the bronchi and lessens secretion. The arterial spasm soon relaxes and dilatation with congestion follows, causing increased secretion. This change renders the mucous membrane more susceptible to infection by microorganisms already present and others brought in by inspiration. The greater frequency of bronchitis in the damp, cold, variable weather of spring and autumn bears out these conclusions. That chilling alone, however, does not cause bronchitis is proved by the experiences of the Nansen and the Shackleton Polar Expeditions in which there were no "colds" or bronchitis even after

swimming in the cold Arctic waters to capture a boat escaped from its moorings. The cold, dry air is sterile so that there were no cases of bronchitis or other infectious disease. In the South Polar Expedition when fresh bales of clothing were opened there was a general outbreak of "colds," as also after the shaking of the ship's carpets due to the bacteria they contained being set free. Recovery in all cases was rapid, due to the dry, pure air. It may be noted that at once on their return home, the men fell victims to one or another of various infections. They had lost their immunity.

Another frequent cause of tracheo-bronchitis is the extension downward of infection from unhealthy conditions in the naso-pharynx. The infection is frequently confined to the trachea and large bronchi, but may extend even to the bronchioles. Those living an indoor life, especially in over-crowded, ill-ventilated rooms, are more subject than those engaged in outdoor, more vigorous occupations. As with other inflammatory conditions, infection is the active cause, hence it follows that in all cases infection from the spray of coughing is a possibility; epidemics of influenza emphasize this fact.

Focal infections in the upper air passages, *e. g.*, in the tonsils, nose, sinuses and teeth, may give rise to local areas of bronchitis. The removal of these local foci is followed by disappearance of the symptoms. The fact is important as such cases may be regarded as tuberculous in origin.

Causes of insufficient pulmonary ventilation, as physical deformity, cardiac and pulmonary diseases, and blood impurities from any source, are often accompanied by bronchitis in a chronic form.

Bronchitis occurs in the course of many general diseases such as measles, whooping cough and typhoid fever; in pneumonia it is frequently but not always present. It nearly always affects the smaller bronchi and not rarely the bronchioles. The infection in such cases is blood borne. The inhalation of fumes of strong acids is a non-infective cause of bronchitis. The vapor irritates the respiratory mucous membrane and causes inflammation, infection usually following later.

The Bacteria of the Normal Air Passages.—The question naturally arises whether the normal air passages are sterile or the habitat of bacteria, as are the mouth and large bowel. Great masses of bacteria are found in the healthy nasal cavities; they may be pathogenic. In the anterior nares, the vibrissæ, and the lower parts of the mucous membrane are rich in bacterial flora; in the upper and back parts, the organisms rapidly diminish in healthy conditions. The mouth and throat contain many organisms of various kinds; the larynx lodges few. In the trachea the number quickly lessens. Most of the small bronchi in animals, and doubtless also in man, are probably free of bacteria, although a few non-virulent ones may occur here and there. After tracheotomy in animals bacteria early enter the trachea and bronchi, and lead to inflammation of the mucous membrane, and often later of the lungs; this must be quite as true also of man.

That in inhalation, especially forced, dust rich in bacteria reaches the finer bronchi and even the alveoli is certain, but in the sound lung the inhaled microorganisms are usually soon removed, made harmless, and

die; while the coal and other dust particles remain in the lung tissue, as well as in the lymph nodes. That these germs which are found here and there in the sound lung and bronchi may, under certain conditions, such as chilling, become pathogenic is possible but probably not frequent. Irritant gases inhaled for a short time by animals produce congestion of the bronchi, with free exudate, but the secretion being sterile is soon absorbed and the mucous membrane restored to normal. If the inhalation is long continued, organisms from the nose and throat, as well as those from without the body, gain entrance to the bronchi and even the lungs, and an inflammation may result.

It is an error to assume that the organisms normally in the nasal cavities are usually the infectious agents in the bronchi and lungs; much oftener the infections are exogenous, the endogenous ones usually lacking virulence. In healthy individuals certain aids to the virulence of most germs are necessary to enable them to excite inflammation in the respiratory tract. Many organisms, especially in the nose, or even in the lungs, die early or become avirulent; others become infective only after their virulence has been increased, or they are aided by favorable conditions.

Though infection plays the important role in diseases of the respiratory passages, yet other factors which aid in the production of the disease should not be overlooked. Wetting and chilling, formerly regarded as efficient causes of bronchitis, pneumonia, etc., have been proved by investigation to be not more than of secondary importance in the production of these diseases. In many cases they play a necessary part, in that they create a condition without which the infecting organisms would be powerless to excite the disease. Bacteria, however, in most instances cause bronchitis without the aid of chill, while chill never causes bronchitis in the absence of infecting organisms. Yet in persons with irritable respiratory tracts, cough, with slight expectoration and without illness, not infrequently occurs after chilling. This is especially true of the nose, throat, and larynx, which are usually not quite normal. That in healthy persons marked chilling in absence of infection causes no injurious results is shown by the experience of Arctic explorers.

Pathology.—The pathological changes begin with dilatation of the vessels of the inner, fibrous coat of the bronchus, followed by œdema and swelling of the basement membrane. Irregular desquamation of the ciliated epithelium follows, which, with rapidly formed new cells varied in size and shape and many leukocytes, are cast off into the lumen of the tube and expectorated with the mucus. The mucous glands are also affected and much mucus and cell elements are added to the bronchial secretion. Some may be inhaled into and excite inflammation of the smaller bronchi. The whole thickness of the bronchial wall may become swollen and infiltrated with leukocytes. The calibre of the tubes is narrowed and in the smaller ones many may be occluded and the related lobules of the lung collapsed. The lymphatic vessels lie in the outer bronchial walls and in the mediastinum; they become swollen, as do also the glands at the root of the lung.

Symptoms.—*Cough* and *expectoration* are cardinal symptoms, except in young children who swallow the mucus, and frequently in feeble old

people in whom bronchial irritability is slight or lost. Inflammation of the trachea and large bronchi causes a feeling of soreness beneath the sternum. Recovery usually occurs in a few days; in some the disease becomes grave and even fatal, a fact that should be emphasized. If there are recurrent attacks, complete recovery of the mucous membrane may not take place and a chronic inflammation results. If the *smaller tubes* are affected, the onset is usually with a feeling of chilliness, a sensation of tightness in the chest and fever. *Cough* is an early symptom. At first it is short, frequent and hacking and often paroxysmal. The irritability of the bronchi lessens as they descend to the terminals, but the muscular irritability increases proportionally, hence the persistence of cough although usually less severe. The *sputum* at first is scanty, viscid and glairy, often with occasional streaks of bright blood. It becomes more abundant, yellowish and muco-purulent and, owing to desquamation of epithelium, increase of gland secretion and of leukocytes, requires less cough to get rid of it. Owing to the narrowing of the tubes from swelling of the mucous membrane and accumulation of secretion, there is some dyspnoea varying with the degree of obstruction. The swelling of the mucous membrane may be so great as to close even the trachea and large bronchi, especially in severe influenza epidemics. The dyspnoea is increased by paroxysms of coughing and on exertion. *Pain* in the chest, chiefly in the axillary region, is quite frequent. It may be caused by local pleurisy, due to infection by the lymphatics from the bronchial walls to the surface of the lung. There may be slight pleural effusion sufficient to cause dulness at the base of the lung.

In the aged, in whom bronchial as well as general irritability greatly decreases, cough is rarely marked as their bronchi are more tolerant of the secretion. Dyspnoea is also less marked. Expansion is more or less restricted owing to rigidity of the chest wall. As a result of these changes in the aged, bronchitis, as well as pneumonia, may progress to a fatal termination without any other symptoms or signs than increasing weakness and somnolence.

In children on the other hand, in whom all functions are highly irritable, cough is frequent, the respiration and pulse increase and fever may be high. The disease usually begins in the smaller bronchi and frequently advances into the bronchioles filling many of them, hence dyspnoea is marked in severer cases. Owing to the elasticity of the ribs and the obstruction to the entrance of air, there is retraction of the lower part of the chest and narrowing of the sterno-costal angle due to the stronger action of the diaphragm during inspiration; at the same time, there is greatly increased expansion of the upper portions of the chest to compensate for diminished action of the lower parts.

If from any cause a bronchus is obstructed, such as by a foreign body, copious exudate or œdema of the mucous membrane, or from œdema of the lung, air is prevented from entering the alveoli, the blood from the affected portion of lung is returned to the left ventricle unoxygenized; it cannot be affected by the most vigorous respiration. If the area of affected lung is small the quantity of anoxic blood will be also small and insufficient to cause perceptible cyanosis or even the slightest lividity;

if large, the anoxemia will be marked in proportion to the area of lung affected and give rise to cyanosis in a greater or less degree.

So long as the amount of the unaffected portion of lung is sufficient to oxygenize enough blood to meet the physiological demand there will be no respiratory discomfort although the breathing may be somewhat deeper and more frequent. The respiratory capacity is lessened and may be easily overtaxed by exertion; if it falls below that point, air hunger will occur. *Anoxemia* is a condition of the blood; *air hunger* a symptom of insufficiently oxygenized blood in the circulation.

Destructive Gases in the World War.—Before the World War, the results following the inhalation of destructive gases were well known owing to accidental spilling of nitric, sulphuric or hydrochloric acid on wood refuse. The gas arising from the contact, even if slight, when inhaled causes great tracheo-bronchial irritation; if strong, it has a destructive action in proportion to its density on the epithelial lining from the larynx to the terminal bronchioles. In the World War, identical effects were produced, from the slightest to the most severe. In the cases in which dense vapors were inhaled the epithelial lining of the respiratory tract was at once destroyed; serous exudate into the tubes followed at once and was churned up into a copious froth that filled the whole respiratory tract and obstructed the entrance of air. Anoxemia quickly followed as shown by cyanosis; in some cases the anoxemia was so marked that death occurred without other apparent cause. At *autopsy* the air vesicles were found filled with coagulated secretion but otherwise unaffected.

Air hunger was not usually extreme and was not materially relieved by oxygen. The inhalation of pure oxygen relieved the anoxemia in a few minutes, the cyanosis disappearing, but strangely had little effect on the air hunger.¹ Oxygen passed through the froth and saturated the hemoglobin but apparently carbon dioxide in the blood plasma could not be eliminated through the froth. Similar results occur in acute pulmonary oedema and the symptoms may be quite as dramatic and terminate fatally even more rapidly. This was well illustrated in an active overworked man aged seventy years. He was indisposed for a few days with a mild bronchitis probably due to influenza, then suddenly a rapid effusion of serum occurred, probably due to pulmonary oedema, into the respiratory tract which was churned into a copious froth that filled the tract from larynx to terminal bronchioles, causing marked anoxemia, dyspnoea, and profuse perspiration. Oxygen inhalation lessened the cyanosis and gave some general relief but death followed within a few hours.

In the adult, *capillary bronchitis* (bronchiolitis) is rare, but occurs oftener in children in whom immunity is probably less. It occurs in areas here and there also in older people, and in persons subject to chronic bronchitis and emphysema. From the more severe infections, as of influenza and measles, it may, however, occur even in vigorous adults.

If the entrance of air is not obstructed the lungs become distended, so that the thorax is expanded to its utmost and is only raised in inspiration. The diaphragm is depressed, and the lungs extend deeply in the

¹ Hoover, C. F.: *Oxford Medicine*, vol. 2, p. 15, 16.

chest. The percussion note is loud and deep; precordial dulness is reduced; the liver is depressed. After death the right heart is found greatly dilated and full of blood; the lung is distended with air and quite dry. The condition is one of marked obstruction to the pulmonary circulation. If the secretion of the larger bronchi is such as to impede the entrance of air, only the upper part of the chest becomes distended, while the lower is retracted and drawn in markedly in inspiration as in laryngeal obstruction. In the lower parts of the lungs areas of atelectasis occur, usually followed by infection, and bronchopneumonia results. In this group belongs the great majority of cases of capillary bronchitis. The rales of *capillary bronchitis* are widely distributed, fine and moist; the breath sounds are often weak and may be absent over some areas.

In primary cases the onset is sudden, as in pneumonia. The temperature may rise to 104° F. or more. Respiration becomes rapid, 60 or more in the minute. Each inspiratory act is short and quick, the expiratory longer and more difficult, and requiring the aid of the accessory muscles of respiration. Fine vesicular rales are abundant and wide-spread, somewhat larger, softer, and more vesicular than the fine crepitant rales which are caused by inflammation of the infundibulum and alveoli. The respiratory sounds are usually weak or absent in several areas of collapsed lobules. Even with a high temperature there may be a cold, clammy sweat. As the dyspnoea increases the expression becomes more anxious, the lips and cheeks show cyanosis, and the alae nasi dilate in inspiration. There is great restlessness, which gradually abates as the cyanosis deepens. In fact the whole picture is that of bronchopneumonia. Until the small pneumonic areas in such cases coalesce to form large masses of consolidation, the multiplicity of fine rales completely obscures the physical signs of pneumonia, yet the diagnosis may usually be made by the general symptoms which become much graver than those of uncomplicated bronchitis.

Diagnosis.—In the adult this is seldom difficult, yet some cases baffle the most skilful. The difficulty is not so much in diagnosing bronchitis as in being certain that it is the primary and only affection, and not secondary to some other disease whose symptoms are latent or masked, as whooping cough, influenza, typhoid fever, or tuberculosis. Much can be done to prevent error by careful examination of the sputum, but even the finding of pneumococci, streptococci, or influenza bacilli in the sputum does not necessarily exclude the existence of some other disease.

A localized bronchitis is usually symptomatic; for example, bronchitis limited to the apex may be the first sign of pulmonary tuberculosis, that of both bases is usually due to hypostatic congestion. Influenza also often causes localized bronchitis. Bronchitis of the larger tubes, especially in children, may be due to irritation from enlarged bronchial glands; in such cases the cough is generally of a violent, convulsive character. A similar cough may be caused by disease of the upper air passages and by foreign bodies in the bronchi. In mitral stenosis the bronchi are very susceptible to infection owing to the obstructed circulation; in such cases the sputum may contain some bright-red blood, often in large quantities, and the affection may be confounded with tuberculous disease.

Incipient pulmonary tuberculosis may simulate simple bronchitis. There is usually a history of gradual failure of health, yet it must not be overlooked that tuberculosis is not rare in stout, florid people, who are apparently in good health and complain of nothing but an irritating cough with scanty expectoration. No signs may be found on examination, or, at most, only a few evanescent, moist, or piping rales at the apex. A hasty diagnosis should not be made in such a case, as unnecessary anxiety may be excited; careful observation is necessary.

Miliary tuberculosis is generally marked by a higher and more persistent fever, more prostration, and greater dyspnoea. The fullest investigation of the sputum, when present, affords, with few exceptions, the most certain basis for a diagnosis.

The diagnosis of *capillary bronchitis* is often very difficult. The dyspnoea, the auscultatory signs, the fever, and the signs of toxemia and asphyxia distinguish it from ordinary bronchitis. It is probable that the lungs are affected in all cases and that the condition is bronchopneumonia.

Bronchitis in the Aged.—The tendency to great exhaustion is the most characteristic feature. There is usually no fever, the pulse is good, and the respiration only moderately quickened. Expectoration is easy as a rule, and the cough, therefore, not excessive. But there is a marked tendency to depression and drowsiness. The nights are restless, appetite is lost, but thirst is usually marked; hence the urine is copious and in the drowsy state is frequently passed unconsciously. The disease is most frequently due to a streptococcus infection, and if not early fatal generally passes into a chronic bronchitis. Many cases terminate in bronchopneumonia, but this develops so insidiously, as a rule, that it may easily escape detection. Cough and expectoration often diminish, the temperature and respiration remain undisturbed, but the pulse grows weaker and more rapid. Owing to the rigidity of the chest wall usually little can be determined by physical examination, therefore, in many old people who have shown no symptoms but prostration with somnolency and feeble pulse, an unsuspected bronchopneumonia is found at autopsy.

Prognosis.—Except in the very young and in the aged, the bronchitis of the larger tubes is rarely fatal, but there is considerable uncertainty as to the duration of the attack and the completeness of recovery. The affection is viewed with too much indifference, and to want of care is often due the frequency with which slight catarrhal affections of the trachea and larger bronchi persist after acute bronchitis. Mild cases usually require ten days or two weeks, and severe ones, especially the streptococcus cases, three or four weeks to make a satisfactory recovery. Even after that the recovery in many is incomplete and they are susceptible to recurrences of cough after slight chills. In the emphysematous, recovery is nearly always tedious, often requiring several months, especially in cold, damp climates.

A fatal termination is rare except in young children and old people, or in patients suffering from such grave diseases as nephritis, heart disease, diabetes, chronic bronchitis, and emphysema; in these bronchopneumonia is a frequent and dangerous sequel. The signs of danger are the evidence that indicate failure of the right ventricle, great dyspnoea, short, ineffective

cough, cold sweats, and a weak, rapid, irregular pulse. There is little hope of recovery in a patient with this symptom-group.

A severe attack of bronchitis in an infant may be fatal in a day; if less severe it may drag on for a week or more before death. In older children the duration is longer and the recoveries more frequent. The unfavorable signs are those that point to failing power in the respiratory, circulatory, and nervous systems, as dyspnoea, lessening in frequency and force of cough and consequent cessation of expectoration, cyanosis, delirium, coma, and convulsions.

Prophylaxis.—Much can be done to prevent catarrhal affections by the adoption of a healthful manner of living. Cleanliness is of the first consideration, cleanliness of air as well as of person and surroundings. Air not being tangible, its purity does not appeal to the masses as do other forms of cleanliness. In the crusade against tuberculosis the necessity of fresh air has been so much insisted on that its importance in the maintenance of health, as well as in the treatment of other diseases, is in danger of being neglected. Next to a vigorous, outdoor life should be placed the daily cool bath, the temperature being graded according to the age and constitution of the individual. The clothing, the bed, the sleeping-room, the avoidance of chill in dressing, and many apparently trivial matters should receive careful attention. All these require attention, not only to keep the healthy well, but also to increase the resistance to recurrences of the attacks in those who have had bronchitis. Unhealthful occupations, especially those in which there is much dust and the air is impure, should be avoided. The dwelling-rooms should not be overheated, nor the air too dry. The clothing should be light, absorbent, and suitable for the season, but burdening with clothes in any season should be avoided. Coddling, as well as irrational exposure, like all extremes, is bad. In all cases the naso-pharynx should receive appropriate treatment, if disease is present, as this is so frequently the source of infection of the bronchi.

Treatment.—In the opinion of most people mild cases of bronchitis do not require any treatment, as they deem it but a slight ailment. They therefore seldom stop work or modify the routine of the daily life, too often with serious consequences.

As the affection is common and there is no specific treatment, it follows that many plans of treatment have been tried, rational and irrational. As in other diseases, the patient rather than the disease should be the object of treatment. As patients differ so much in vigor and constitution, it is not surprising that various and even opposite plans of management should often prove equally successful in attaining the object aimed at. No uniform course of treatment can be the best for all, so that each case should be considered on its own merits. Our aim is to secure arrest of the affection and the removal of its effects in the shortest possible time. Beyond symptomatic treatment little can be done by way of cure. In all cases the patient should remain in bed in a warm well-ventilated room, or better, on a balcony if the cold air does not cause excessive cough. For the adult, quinine, acetyl salicylic acid, each gr. ii (0.15 gm.), acetanilide gr. $\frac{1}{2}$ (0.03 gm.), given every two or three hours for a few times is highly regarded by many for relief and lessening the duration of the attack.

A Turkish or hot bath followed by hot applications to the chest often gives comfort. For troublesome cough, Dover's powder, gr. v to xv (0.3 to 1 gm) is usually effective; it also promotes secretion by relaxing the arterioles. Codeine gr. $\frac{1}{4}$ (0.016 gm.) is also useful. Compound tincture of benzoin in a steam atomizer, or camphor and menthol each gr. iii (0.2 gm.) to 1 oz. (30 cc.) of liquid paraffin in an atomizer, applied through the nostrils, or, better, the throat if well exposed, and used frequently, are useful in soothing irritability of the mucous membrane and in lessening the tenaciousness of the secretion. The patient should not be up until the fever, if any, and general symptoms are quite relieved, and even then chilling, fatigue and impure air should be avoided. Due consideration should be given to the vigor and age of the patient, the aged and children requiring the greatest care. Even in vigorous adults this disease sometimes becomes grave, and is not as trifling as it is generally regarded.

Inhalation of weak chlorine vapor suggested in the hope of promptly arresting catarrhal infections of the respiratory tract so far has not proved successful.

In *general bronchitis* the gravity of the disease increases as it extends down the bronchial tree, especially in the aged and children in whom life virtually depends on the effectiveness of cough in getting rid of the secretion. Opium and similar sedatives therefore become vastly more dangerous than in disease of the large tubes. Frequency of cough prevents sleep, so that a sedative may be craved in order to get some rest, but loss of sleep is much less dangerous than the accumulation of mucus that must occur in severe cases if cough is abated. Dyspnoea with any degree of cyanosis and stasis in the base of the lungs are signs of dilatation and engorgement of the right ventricle and forbid any sedative. Instead, a free action of the bowels by a purgative, or, probably better at least in the adult, a large enema followed at once by 1 cc. of pituitrin injected intramuscularly may prove more effective by not only emptying the colon and reducing abdominal fulness, giving the diaphragm greater freedom of action, but also stimulating the heart muscle as well as that of the intestine.

As in all prevalent diseases, a great many drugs have been recommended for treatment, but few, if any, of them are of much benefit.

As regards applications to the chest, the extremes of heat and cold, with all variations between, are used. Both heat and cold often give effective relief, but cold has the advantage in that it is more easily applied, and that it excites deeper inspiration. *Cold* is most easily applied by using a *compress* of two to four layers of gauze, old linen or cotton, cut large enough to cover the whole chest; the compress is wrung out of cold water, applied closely so as to be in intimate contact with the surface of the chest and covered with a dry, thin flannel, to permit of evaporation. The coldness of the water and the frequency of changing the compress must be regulated according to the patient's strength and the urgency of the symptoms. The *cold, wet pack* is useful for nervous patients.

Heat is usually applied by a poultice of linseed meal, with or without mustard. The poultice, to be effective, must be applied very hot, burning being prevented by a layer or two of flannel placed beneath it, and the

whole covered with flannel, waxed paper, or rubber cloth to retain the heat as long as possible, and hold the poultice in close contact with the chest. The whole front of the chest should be covered with the poultice, which should be changed on cooling. It is difficult to accurately estimate the value of poulticing, but that the benefit derived from its use is much less than is generally supposed by the profession and public there is no doubt. Chief among the objections to its use is the great weight.

Free perspiration, especially at the beginning, often moderates and not rarely aborts an attack. A full warm bath, at a temperature of 100° to 105° F., for ten to fifteen minutes, is usually effective. The patient should be at once placed in a warm bed, and diaphoresis encouraged by giving hot drinks. Hot bottles may be put around the patient.

In adults, except the aged, *venesection*, if there is a rapid flow of blood but not necessarily a large quantity, should improve respiration and lessen cyanosis by relieving the dilated right ventricle, slowing the heart beat and lessening general distress.

Inhalation of oxygen may be of much benefit, at least temporarily, the mask being held closely over the nose and mouth. It may cause less irritation if passed through alcohol in a bottle standing in quite warm water. If cyanosis is partly or wholly due to pulmonary œdema, oxygen will fail to give relief in proportion to the degree in which the œdema is the cause of the anoxemia as exudate in the air vesicles prevents the absorption of the oxygen. This was well illustrated in a case of pneumonia affecting a large part of the left and the lower lobe of the right lung but without bronchitis. There was marked air hunger but no cyanosis until another portion of the less diseased lung was affected with bronchitis as well as pneumonia but not yet consolidated. The blood from this portion of lung in which the circulation was not yet arrested, returned to the heart insufficiently oxygenated and cyanosis occurred. With oxygen inhalation the anoxemia was at once relieved and the cyanosis disappeared but there was no effect on the air hunger owing to the large volume of lung consolidated.

Strychnine should aid by stimulating the respiratory centre. Digitalis, about 20 minims (1.3 cc.) of the tincture given every four hours for a few doses, may improve the heart's action.

If the continued cough is exhausting the patient, a mild sedative such as a bromide, gr. 10 to 15 (0.6 to 1 gm.) or chloral hydrate, gr. 5 to 10 (0.3 to 0.6 gm.), may relieve it sufficiently to allow one or two hours sleep, by which time the patient should be thoroughly aroused and cough excited so as to get rid of as much secretion as possible.

Good nursing is of the greatest importance. The room should be well ventilated and of uniform temperature. Cold air is preferable if it does not unduly increase cough as it stimulates general vigor as well as giving a denser air to breathe. If notwithstanding such means, secretion increases, an emetic may give relief. If its action is favorable it may be repeated, if not it will do harm and should death follow soon afterward it may be attributed to the emetic rather than the disease.

The diet should be light and nutritious and given at short intervals, especially at night when there is natural depression of the vital powers.

Autogenous *vaccines* in cases of slow convalescence and of recurrence may effect a complete cure. The vaccine should contain the chief organisms present in the sputum.

CHRONIC BRONCHITIS

Etiology.—In America, with its dry climate, chronic bronchitis is relatively infrequent, whereas in Britain, with a climate moist and often cold, the disease is very prevalent and frequently grave. Chronic catarrhal inflammation develops most frequently in those who suffer with repeated attacks of acute or subacute bronchitis. After each attack complete restoration of the mucous membrane of the trachea and large bronchi does not take place, the recovery being less and less complete after each attack until the persistent condition is established. Coördinate conditions, as emphysema, pulmonary fibrosis from tuberculosis or other causes, alcoholism, chronic renal disease or dust-laden air, any or all of which may create a passive congestion, have an important influence in aggravating the inflammatory changes.

Pathology.—The condition of the mucous membrane varies with the degree and duration of the inflammation. The milder and more recent cases differ little from the acute except that the inflammation penetrates more deeply and the secretion is more purulent. The mucous membrane is cedematous, reddish or dark, owing to the full dilated bloodvessels; it is infiltrated and covered with muco-purulent secretion. All the bronchial walls may be infected and the seat of a greater or less degree of leukocytic infiltration. In the advanced cases the mucous membrane is irregularly thickened, partly owing to infiltration and partly to the formation of new fibrous tissue, which may extend into the peribronchial structure and lead in time to fibrosis of the adjacent lung tissue. Long-continued inflammation may lead to destructive ulceration of all the coats of the bronchus, which may dilate, forming a bronchiectatic cavity with profuse purulent secretion; or the inflammatory products may become absorbed, together with all the structures of the bronchial wall—mucous membrane, muscular coat and cartilages—leaving a thin, dilated bronchus (Adami and Nicholls).

Symptoms.—In general, they are those of bronchitis without the acute symptoms; in fact, it is often difficult to differentiate between mild, recurring attacks of acute bronchitis and the chronic variety. In most cases, the affection begins in the damp, cold seasons as a troublesome morning cough which persists until the night's secretion has been expelled followed by relief for the remainder of the day. The sputum may be scanty, but later it is often copious, muco-purulent and yellowish, and may sink in water like that of chronic pulmonary tuberculosis, or it may be thin and serous.

If there is little or no emphysema, which exists in all protracted cases, the breathing is normal; the general health is good and quite equal to an active life. In a few years in most cases the relief which occurs in summer grows shorter and less complete; the cough in winter becomes more severe and the general health begins to fail. When the disease is of a more severe

type it affects the smaller tubes early; all the symptoms are more marked, the cough is more severe, and may be paroxysmal. It becomes paroxysmal and labored, if the secretion is abundant and adhesive. Dyspnœa in some degree is never absent in the later periods; it is due to the emphysema and pulmonary fibrosis which always develop.

Slight causes are apt to excite exacerbations of cough, and necessitate confinement to the house or room for a few days. In the intervals, however, the general health is good. In more severe and advanced cases the symptoms are much worse, cough becoming more troublesome at night and expectoration profuse, purulent and occasionally offensive; in rare cases it is serous. There may be frequent recurrences of fever due to fresh attacks of bronchitis, or to disease other than of the respiratory organs. Emaciation, loss of strength, night-sweats, loss of appetite and disturbed digestion in varying degree are usually present. In advanced cases the right ventricle begins to fail, as shown by cyanosis, enlargement of the liver, distention of veins or clubbing of the fingers. Later, cardiac dropsy supervenes, the urine becomes scanty and albuminous, the weakness becomes so great that the bronchial secretion cannot be expelled, and death follows.

Besides the ordinary muco-purulent bronchitis, which is much the most common, there are other clinical varieties deserving special notice.

1. *Dry Catarrh* (Catarrhe sec of Laennec).—This is rather rare but Laennec considered it frequent; he probably included the cases of winter cough already described. From time to time in the muco-purulent variety there may be cessation of secretion and then the symptoms are those of dry catarrh.

Dyspnœa is marked, and there is severe paroxysmal coughing with a little sputum, which is found to contain numerous small, pearl-like masses of tough mucus, with pus cells and blood corpuscles in its meshes. Charcot-Leyden crystals and Curschmann's spirals are often present. The cough often causes acute tearing pain referred to a spot at the attachment of the abdominal muscles to the lower margin of the thorax. On *auscultation* there are many piping rales with hissing sounds; there may also be moist and creaking rales. Later the dyspnœa becomes continuous, owing chiefly to the emphysema, which nearly always develops; the course is marked by paroxysms like those of asthma, in which the wheezing and piping rales are marked all over the chest.

2. *The Serous Form*.—This, also first described by Laennec, is rare. It is distinguished by the expectoration of profuse, muco-serous, translucent, colorless sputum, which separates into an upper frothy layer, and a lower clear one like egg albumen or gum arabic mixed with water. The rarity of this affection is shown by the few cases reported in recent years, and the variety in the descriptions given of it by different writers. West describes an acute and a chronic form.

The *chronic form* is commonly preceded by ordinary catarrh, and once established, it is usually intermittent. During the twenty-four hours several pints may be expectorated, often in copious quantities at short intervals. It may persist for years without change in character, and the patient's general condition be little affected; some cases are

probably of the nature of a nervous hypersecretion. It may occur as a terminal phenomenon in acute tuberculosis, pneumonia, pleuritic effusion, cardiac disease, etc. Occasionally a profuse serous discharge occurs in cases of thoracic aneurism or mediastinal tumor. It may occur after aspiration of a pleural effusion and prove fatal from filling of the bronchi with serous fluid. The patient is drowned in his own secretion.

3. *Purulent Bronchitis*.—This is more or less marked in the final stage of all cases of chronic bronchitis, but there may be a marked purulent sputum from the first, a pint or more being expectorated in the twenty-four hours, as if a large cavity or an empyema had ruptured into a bronchus. The pus may become offensive but the odor soon abates; the odor is less marked than in putrid bronchitis. Purulent bronchitis may become converted into the putrid variety, especially if bronchiectasis develops. As a rule the patients lose flesh early, but the course is usually chronic.

Diagnosis.—In all cases of *chronic bronchitis* of whatever kind, the most important question is whether the condition is not due to or at least associated with tuberculosis. If the sputum is carefully examined, it is remarkable how often the tubercle bacillus is found, even although the course has been fever free and all the indications point to ordinary chronic bronchitis. The sputum, however, may not contain bacilli, and emphysema may obscure the signs of local changes. In doubtful cases a tuberculin test will generally give positive evidence if tuberculosis exists, which may, however, be located elsewhere.

Prognosis.—In the young the outlook is often hopeful, even when they are emphysematous and subject to attacks of dyspnoea. Many improve as they grow older, and in time the symptoms may completely disappear. After middle life there are few recoveries, but many are able to lead comfortable, useful lives, and may attain advanced age, unless carried off by some intercurrent affection. In the severer cases various complications are certain to arise in time. Of the complications general *emphysema*, the most common, is rarely absent. It increases the dyspnoea as well as the liability to recrudescences of the bronchitis. *Interstitial fibrosis* of the lungs is common, and may lead to the gradual development of bronchiectasis. Much weight should be attached to the state of the cardiovascular system, as in the late stages the chief danger is from failure of the right ventricle.

Treatment.—It is of the first importance to avoid a cold, wet, and foggy climate; but it is in just such climates that the affection is most frequent, and, unfortunately, most sufferers are unable to seek a better one. A mild sea air is usually most beneficial in the winter, such as Nassau, Bermuda, Jamaica, Cuba, Florida, and Southern California in America; in Europe, the Mediterranean Coast, Sicily, Madeira, the Canary Islands, and the Isle of Wight. Some patients, especially those with tuberculous tendencies, do better in a dry, warm climate, such as Mexico, New Mexico, Arizona, and Colorado; and in the East the higher parts of Georgia and the Carolinas. Not rarely it will be found best to try moist and dry climates alternately.

In the summer months a more bracing climate will usually be found most beneficial if a continuous outdoor life is led, especially in the forest

districts or on the plains. In Canada, Muskoka, the forests of Northern Ontario and Quebec, the plains of the Northwest, the foot-hills of the Rocky Mountains, and many parts of British Columbia offer admirable opportunities for such a life. In the United States, the New England and the Pacific Coast States are the best. Experience has proved that all these parts afford excellent resorts for tuberculous patients, and they should be equally favorable for chronic bronchitis, but as yet little consideration has been given to the subject. In time it will probably be shown that in chronic bronchitis, as in tuberculosis, the all-important matter in the treatment is not the mild climate, but the outdoor life, care being taken to keep the body and limbs warm so as to prevent congestion of the bronchial mucous membrane. Even in the Yukon, long-standing cases of chronic bronchitis have quickly recovered.

If the patient is unable to leave home, no effort should be spared in improving the general condition. This will necessitate as much outdoor life as possible. The clothing should be light but warm so as to prevent chilling of any part. Mouth breathing should be avoided, and, if necessary, a respirator worn to warm the air.

The closest attention should be given to the functions of excretory organs, so as to counteract the strong tendency that exists in many of these cases to the accumulation of waste products in the blood. The diet should be ample for the needs of the patient, but excess should be avoided. Cod-liver oil, if it does not disturb appetite or digestion, benefits many, especially those of spare habit.

Autogenous *vaccines* should prove of much benefit in all cases, especially if given before the bronchi have undergone organic changes.

The *cough* is usually more frequent in the morning, less so on lying down at night, and not rare during the night; it is often relieved by giving bicarbonate of soda in warm milk. At Brompton Hospital a combination of sodium bicarbonate, gr. xv (1 gm.); sodium chloride, gr. v (0.3 gm.); spirit of chloroform, ℥v (0.3 cc.), in anise water, added to an equal quantity of warm water, is the usual combination administered. If the sputum is scanty and viscid, ammonium carbonate and potassium iodide, of each gr. iij (0.2 gm.), may be added.

Hydrotherapeutic measures suitable to the individual have proved of much benefit. These are best carried out at a properly equipped institution, but many can be utilized at home. The Turkish bath, or a portable hot-air or vapor bath in the bedroom, if used promptly at the beginning of an intercurrent acute or subacute attack, often aborts it. It should be followed by a warm bath. A full warm bath of itself may be equally effective; it is more easily given and in the aged less likely to cause depression. The feeling of oppression and tightness in the chest is greatly relieved as soon as sweating begins. After the bath the patient should be rubbed dry and at once put into a warm bed in a warm, well-ventilated room. A respirator may be worn during the night, the sponge being lightly saturated with terebene, menthol, or eucalyptol. These and similar measures, especially hydrotherapeutic ones, will go far to obviate the necessity for internal medication.

If acute attacks occur, they are to be treated as indicated in acute

bronchitis. The more depressing remedies are, however, rarely advisable and should not be given to the feeble or the old. If the secretion is viscid and scanty, the use of alkaline fluids in a fine atomizer, better the nebulizer, may give much relief. Inhalations of the vapor of hot water to which have been added eucalyptol, menthol and compound tincture of benzoin, may be tried.

These and similar drugs may also be given internally. Terebene, $\text{m}\times$ (0.7 cc.), is probably the most valuable if expectoration is profuse. Turpentine, $\text{m}\times$ (0.7 cc.); creosote, mij to ijj (0.13 to 0.2 cc.), and terpene hydrate, gr. ij to v (0.13 to 0.4 gm.), are also much used. Copaiba is regarded by many as the most effective of the balsams. Its volatile principle is eliminated by the respiratory mucous membrane, modifies its secretion, and acts to a certain degree as an antiseptic. Tar has been recommended as an addition, gr. iv (0.25 gm.) of each being given in capsule four to eight times a day. Balsam of Peru and of Tolu, benzoate of soda and many others have also been used.

All these remedies produce similar results. If badly borne by the stomach they may be administered by inhalation. A spray or the dry fumes of chloride of ammonium is often of much use. These remedies may be used as an addition to the turpentine group.

In long-standing and inveterate cases, intratracheal injections may be used as recommended in bronchiectasis. The *postural method* aids in expelling the secretion when abundant and in preventing dilatation of the bronchial tubes. If the foot of the bed is well raised, so that the upper part of the chest is lower than the base, the drainage of the secretion from the bronchi not only aids rest, but relieves the mucous membrane of the continued irritation of its own secretions, one of the chief causes of the persistence of the inflammation.

Local applications to the chest, cold compresses or linseed poultices, with or without mustard, according to indications, are advisable. In the intervals between attacks, liniments are usually preferred, such as tincture of iodine, ʒss to j (2 to 4 cc.) to 1 ounce (30 cc.) of turpentine liniment, applied at night until moderate irritation is produced.

These measures usually suffice to control the cough if it is due to the secretion rather than to excessive irritability of the mucous membrane. In the latter case something more sedative is needed. The addition of 15 to 20 drops (1 to 1.4 cc.) of chloroform to the inhalation may moderate the cough; if not, one of the bromides may be added to the warm alkaline mixture already specified. If this is insufficient, heroin or codeine will have to be given until the cough is sufficiently controlled, due caution being taken that necessary cough is not interfered with; or paregoric may serve the purpose better, as the camphor stimulates the circulation of the debilitated and aged. Whisky at bedtime, especially in the aged, often serves the double purpose of quieting the cough and aiding sleep.

The treatment of *asthmatic attacks* occurring in the course of chronic bronchitis will depend on their character. The more purely spasmodic they are, the more effectively will morphia hypodermically relieve them, but it is a dangerous remedy if there is much secretion. In the latter cases "the drugs of greatest value are potassium iodide, gr. viij to xv

(0.6 to 1 gm.); extract of stramonium, gr. $\frac{1}{4}$ (0.016 gm.), and the ethereal extract of lobelia, m20 (1.3 cc.), in combination with stimulant expectorants, such as carbonate of ammonia, gr. iij to v (0.2 to 0.4 gm.), or ether" (Fowler). As there is general venous fulness a saline purgative sufficient to cause a free action of the bowels will be of much benefit.

In those in whom there is damage of the heart, the greatest dependence must be placed on cardiac stimulants and digitalis should be taken in short courses from time to time. Exercise in the open air, but not beyond the powers of the patient, so as not to overstrain the heart, is probably the best of all cardiac tonics. Respiratory gymnastics are of much benefit; as are also daily cold baths, provided they are followed by a feeling of exhilaration. Similar treatment is called for in the corpulent, in whom the bronchitis may be due to defective circulation.

In alcoholics, the failure of circulation is the chief cause of bronchitis but toxemia is important. In their treatment, in addition to improving the heart's action, it is necessary that the taking of alcohol be much reduced or stopped, and the digestion and excretion aided as far as possible.

In the advanced stage of chronic bronchitis with dyspnoea and cyanosis from failure of the right ventricle, temporary relief may follow a rapid venesection, 10 ounces or more of blood being taken in a full stream. Cardiac and general stimulants, such as pituitary extract, strychnine, digitalis, and caffeine should be given according to the individual needs. Inhalations of oxygen may give relief.

If respiration is impeded by the accumulation of secretion in the bronchi and suffocation is threatening, an emetic may afford temporary relief through the act of vomiting expelling the secretion. In the debilitated condition of these patients it is a dangerous remedy. As in all these cases there is labored expiration due to emphysema, compression of the chest during expiration by the hands applied over the axillary regions should be made several times a day to assist in expelling the secretion. This should be carried out while the patient lies prone with the shoulders hanging over the side of the bed or couch. Proper *posture* during the night may lessen this accumulation of secretion.

Respiratory gymnastics of any form are valuable in chronic bronchitis. They should be carried out in air that is pure and free from dust. They are best carried out without apparatus. Deep inspirations followed by long and forced expirations are useful exercises for anyone who patiently perseveres in their use.

SECONDARY BRONCHITIS

Bronchitis is a frequent complication of a variety of diseases. As a rule the symptoms and physical signs do not differ from those in primary bronchial affections.

1. **Bronchitis in Febrile Diseases.**—In *measles* some bronchitis is always present, so that it may be considered an essential part of the disease. As the smaller tubes are usually affected, it is from the bronchitis, and especially bronchopneumonia, that the chief danger arises in many cases.

In *typhoid fever* slight bronchitis is of frequent occurrence in the initial stage of the disease. By some this initial bronchitis has been attributed to the localization of the typhoid bacillus in the bronchial mucous membrane. Late in the disease, when the heart becomes weak and toxemia pronounced bronchitis may occasion much anxiety; it is caused partly by the toxemia and partly by the defective circulation. The symptoms in such a case are due to hypostatic congestion as well as to the bronchitis and there is much danger of bronchopneumonia.

As a sequel to *whooping cough*, bronchitis with collapse of lobules is frequent; it may cause a paroxysmal cough similar to the original disease. The bronchitis of *influenza* is of special importance owing to its frequency of occurrence and its influence on the mortality of the influenza. The mucous membrane of the trachea and bronchi shows the usual changes of acute catarrh. The secretion, especially of the smaller tubes, at first is viscid and often blood-stained. The inflammation is very prone to extend to the deeper structures of the bronchial wall; this accounts for the frequency with which influenzal bronchitis is followed by bronchiectasis. The cough is usually frequent, short, dry, very persistent and difficult to relieve. The severity of the general symptoms will depend upon the extent and size of the bronchi affected. If the inflammation extends to the capillary tubes the respiratory symptoms will be severe and it will be difficult to determine that bronchopneumonia has not developed. It may be confined to any part of the lung, and, therefore, difficult to distinguish from tuberculosis.

Treatment.—This does not differ from that of other forms of acute bronchitis. There should be due appreciation of the gravity of the affection, of its long duration in all marked cases, and its liability to terminate in chronic bronchitis and bronchiectasis.

2. Bronchitis in Heart Disease.—This is of great importance, both as a sign of the existence of the affection of the heart and of the impending failure of its function. The bronchitis in *mitral insufficiency* is the one most often seen and most important. It generally affects both lungs and is chiefly due to hypostatic congestion. It is characterized by small, moist rales which are marked at the base, and diminish rapidly from below upward. There is ordinarily a small quantity of effusion into the lower part of the pleural cavities. It is of progressive character, slow in development, and without sudden accessions. It causes gradually increasing dyspnoea exaggerated by slight exercise. The cough is variable but fatiguing even when not severe. The sputum is muco-purulent and varies in quantity; in it are found the so-called *cardiac insufficiency cells*. These are large cells containing reddish or rust-colored pigment from blood; in health these cells contain black pigment. They probably come from the alveoli, as they resemble the epithelium normally found there. They are found almost constantly and in such numbers in hypostatic congestion from heart disease that they have been regarded as quite characteristic, but they occur also in the sputum of bronchitis and asthma. They are characteristic only of hypostasis in which the cells become full of pigments.

In *mitral stenosis* there are frequently recurring attacks of bronchitis

in many cases. At first these attacks are slight and the expectoration consists of frothy mucus; later it often becomes tinged with blood. If the right ventricle becomes well hypertrophied, free hemoptysis is frequent and may prove fatal. In such a case due to mitral stenosis, at autopsy the pulmonary arteries showed marked atheromatous degeneration, and were greatly dilated even to their smallest branches. The right ventricle was very greatly hypertrophied but not dilated. In *diagnosis* the error is often made of mistaking mitral stenosis for pulmonary tuberculosis, chiefly on account of the hemorrhagic sputum, but also because of the anemia, absence of cyanosis, and late dropsy of mitral stenosis. A careful examination should prevent the mistake.

Bronchitis in affections of the myocardium and of the aortic orifice and in the course of arteriosclerosis is probably due, in the early stage, to renal disease, and later to myocardial insufficiency.

Treatment.—This should have for its first object the improvement of the circulation. The patient should be at rest, and the diet should be dry in order to add as little as possible to the volume of the blood, which is already too great. Heart stimulants, especially digitalis, will be required to strengthen the heart and increase excretion by the kidneys; purgatives will be of use chiefly by lessening the volume of the blood. In conditions of weak and irregular heart with sleeplessness, morphia hypodermically is usually the best remedy and its use is seldom attended with danger in this form of bronchitis. Potassium iodide may do good by acting on the bronchial mucous membrane, rendering the expectoration easy and quieting the cough. If there is œdema, diuretin or theocin may be effective. The diet should be salt-free.

3. **Bronchitis in Renal Disease.**—Three forms have been described: (a) A simple and common form attended by migratory and fugitive bronchopulmonary œdema. The cough is slight, but dyspnœa of greater or less degree requires treatment. This dyspnœa is paroxysmal, but is not increased by movement and is worse at night than in the day, often attaining a severity sufficient to cause orthopnœa—the so-called “renal asthma.” On careful auscultation over one or several areas, crepitant rales are audible; these areas may be found anywhere. They never occupy a whole lobe. The rales are fleeting and may change from place to place during prolonged auscultation; rarely they persist in the same place for several days. If localized at the apex they simulate tuberculosis. This form occurs without fever and is of short duration, but may recur with great facility.

(b) The second form constitutes what is properly called *albuminuric bronchitis*. It occurs in chronic cases, develops suddenly, and may attain great intensity. The dyspnœa is intermittent and paroxysms are frequent. The cough is frequent, increased during the paroxysms, and accompanied by muco-purulent expectoration, often with blood intimately diffused or in filaments. This form occurs without fever, disappears after a certain time, and is liable to recur.

(c) The third form gives the impression of a veritable *bronchopneumonia*. The onset is often brusque, with fever. The cough is severe and frequent, and increases for several days. The expectoration is abundant

and sometimes sanguinolent. The oppression is marked and continuous, with paroxysms. There are generalized bronchitic rales; after these disappear areas of persistent crepitation are still left. The affection begins in the large and descends to the small tubes, thus showing that the persistent areas are pneumonic. In the final stage of chronic nephritis, a diffuse congestion and œdema often occur, with large, moist rales, due to the stasis of the mucus in the bronchi, and caused chiefly, if not wholly, by cardiac failure.

Causation of the Bronchitis of Cardiac and Albuminuric Affections.—The causes in these two affections are closely allied. Passive congestion and œdema affect the bases of the lungs; they are the mechanical result of the enfeeblement of the heart that is the rule in cardiac cases and frequent in chronic nephritis. The variable and fleeting congestions and œdemas are evidently due to *vasomotor disturbances*. In chronic nephritis they are doubtless caused by toxins acting on the vasomotor nerves of the bronchi, or on the centres in the medulla.

"Renal asthma" is a term of very uncertain significance and applied to dyspnoea arising from a variety of causes. Occasionally in chronic nephritis there are paroxysms of dyspnoea that cannot be distinguished from true asthma and are probably due to the same cause. But the term renal asthma is not confined to these cases, but applied to all kinds of dyspnoea occurring in chronic nephritis in which sudden attacks of difficult breathing, especially at night, are quite common. These attacks are often due to uremia but probably more frequently to disturbed circulation in the lungs and nervous system. Bronchitis in some degree always coexists and aggravates the dyspnoea.

The treatment is such as is best for the renal affection: milk diet if there is no œdema, otherwise dry diet; free action of the bowels; potassium iodide in suitable cases. These means usually ameliorate the bronchitis as well as act favorably on the renal affection. Dry cupping of the chest may do much good, many cups being applied to all parts of the chest, front and back. They may be repeated two or three times a day. Sedatives are often injurious. As cardiac affections usually coexist with the renal, both conditions should be considered in the treatment.

TUBERCULOSIS OF THE TRACHEA AND BRONCHI

Tuberculous infection of the trachea and bronchi is generally regarded as secondary to pulmonary tuberculosis and is not usually treated as a separate disease. In the trachea and at least the larger bronchi the disease is rare except near the end of life, and even then it is far from frequent. This relative immunity is accounted for by the following conditions: (1) The trachea and bronchi form simple, smooth, open tubes, whose walls never come into contact or present irregular cavities in which sputum can lodge and be compressed. (2) Their surfaces are protected by a layer of mucus which is being constantly moved upward by the strong ciliary motion of the epithelium. For this reason the surface never presents any deposits of carbon particles, even although the respired air be laden with them. (3) The tracheal and bronchial mucous mem-

brane is highly sensitive and excites reflex cough when irritated by foreign substances.

In the pulmonary affection the sputum is hurried along so rapidly as to prevent infection of the healthy membrane, and render it infrequent even in the abraded areas, which are usually protected by a thick layer of mucus. Toward the end of life irritability is lessened and the sputum, travelling more slowly, destroys more frequently the less resistant epithelium, so that the bacilli often find an entrance. The posterior walls are infected most frequently because in the bedridden they are the more exposed.

Two processes have been demonstrated pathologically, viz., tuberculosis of the bronchi and tuberculous or caseous bronchitis. Clinically, neither one is known, both being obscured by the more important coexisting pulmonary symptoms. The bronchial wall becomes infiltrated with small cells, causing considerable thickening, and the area of infiltration is soon converted into a yellowish-white, well-defined mass. The epithelium is destroyed early, and the mass, unless the process becomes arrested and absorption takes place, degenerates and is discharged into the bronchus, leaving a small, caseous ulcer. The tendency of the process then is to penetrate more deeply and excite peribronchial inflammation and later involve the lung tissue itself.

Leprosy also occurs in the bronchi, and presents changes similar to those of tuberculosis bronchitis.

TRACHEO-BRONCHIAL SYPHILIS¹

Syphilis of the respiratory tract is apparently rare but it is possible that many cases are overlooked because its possibility is not considered. It may cause superficial ulcers, "mucous patches," throughout the length of the trachea, less often also of the primary bronchi; similar ulcers may form in the larynx. Gummata may form in the mucous and submucous tissue, causing considerable swelling. The superficial ulcers, on healing, leave puckered scars. Gummata may be absorbed and thin smooth scars result. If they disintegrate deep ulceration occurs, often destroying the cartilages, followed by the formation of much cicatricial tissue, which in contracting, may cause marked and irregular stenosis of the trachea, or a bronchus, or of both. The infection may however invade any or all parts of the bronchial tree giving rise to general bronchitis. Severe and recurring hemoptysis without cough or physical signs or symptoms is suggestive of a syphilitic cause.

If the *diagnosis* is in doubt, a search for bacilli and a Wassermann test should be made. If tubercle bacilli are found and the test is positive, the cause is still uncertain. In such circumstances, treatment for the syphilitic infection should be carried out as, in any case, it will improve the general condition and promote the cicatrication of the ulceration if it is due to syphilis.

¹ See also Volume II, page 414.

MUCO-MEMBRANOUS (FIBRINOUS) BRONCHITIS

This affection is characterized by the occurrence of a coagulable bronchial exudate from which are formed cylindrical or solid casts of the bronchial ramifications. It is rare and up to 1869 Lebert found only 44 undoubted cases in the literature. In 1889 West found 54 more cases, and Bettmann in the literature from 1869 to 1902 found 145 cases (including West's), making, with Lebert's list, 189 in all. The occurrence of casts was known to Hippocrates, Galen, and other ancient authors.

The membrane consists of coagulated mucins, contains no fibrin and is therefore to be distinguished from fibrinous casts of the bronchi not rarely occurring in diphtheria cases. It is probable also that there is no bronchitis except as a sequel due to subsequent infection of the injured epithelium of the mucous membrane. Muco-membranous exudate in the colon and the uterus are of identical structure and are probably due to similar causes.

Etiology.—The disease may occur at any age, but is probably rarest in old people. Like bronchitis, it is most common in cold, damp climates, and therefore in the cold season of the year. Muco-membranous bronchitis occurs in association with a great variety of diseases, so various, in fact, that the association appears accidental. The largest number occurred in persons with pulmonary tuberculosis and heart disease. It has been met with in the course of various infectious diseases, such as pneumonia, measles, scarlet fever, erysipelas, typhoid fever, variola, rheumatic fever and influenza. A few cases have occurred in association with asthma, Graves' disease, and pulmonary oedema following thoracentesis. Some, however, occur without the association of these diseases. French observers have found a substance—mucinase—in the blood of these patients that causes coagulation of the mucin, which if freely secreted may give rise to the formation of casts in the bronchi. If this is true the occurrence of these cases would be explained. In any case the condition is not due to infection or inflammation of any origin.

Pathology.—Little is known as to the pathology of fibrinous bronchitis. It seems certain that a variety of agencies may cause a membranous exudate. There is no doubt that the pneumococcus and diphtheria bacillus may cause membranous exudate in the bronchi as elsewhere, but whether other microorganisms cause it also is uncertain. It is also uncertain whether all cases are due to bacteria, as no microorganisms can be found in some specimens. The exudate may form solid casts of the bronchi, or hollow cylinders, or both may be present in the same case. The casts from the small bronchi are probably always solid and from the larger ones hollow. The inclusion of air bubbles may give the casts a beaded appearance. The exudate may be produced in a few bronchi only, or occur in several areas in one or both lungs. Nearly all the casts in museums have been coughed up, few being found in the bronchi at autopsy.

Casts vary in length from 1 inch or so up to 6 or 7 inches, with branches corresponding to the divisions of the bronchi from which they are expelled. They are pearly-gray or white in color, the larger firm and the smaller

softer in consistence. The larger are laminated, the inner layers showing foldings due to the forcing of the older layers farther and farther from the bronchial wall by the successive deposits on the mucous membrane beneath them.

Symptoms.—Dyspnœa, cough, and the expectoration of casts or flakes are the essential features, the presence of casts in the sputum being the characteristic one. The following case gives a good illustration of the symptoms: The patient was a female, aged twenty-seven years. The bronchial attack, for which she first sought advice in November, began in the late summer. She had a dry, irritating cough, with little sputum, and at times coughed severely for several days after which she vomited some white substance. During the consultation she had a severe paroxysm of coughing and brought up a white mucous mass which, unrolled in water, proved to be a hollow cast and several flat pieces from a bronchus,

FIG. 7



Cast from a case of fibrinous bronchitis.

and many solid branches from the bronchioles. During the following three months she had four marked paroxysms, in one of which she coughed up almost a complete cast of the bronchi of the lower lobe of the left lung, considerably larger than the one shown in the illustration. In the intervals between the paroxysms the sputum consisted of a moderate quantity of milky fluid often containing small white pieces of membrane. All the paroxysms occurred in the morning, beginning with chilly and shivering sensations, and in the afternoons there were hot flushes and chilly feelings. Her throat was dry, the cough was irritating, and increased by the slightest exertion. After a day or two casts would be brought up and she would improve; a slight cough continued and the physical signs over the lower part of the left lung persisted. There was slight but varying dulness, most marked before and diminishing after the expulsion of the casts. Coarse crepitations were audible, beginning about the middle and continuing to the end of inspiration, apparently due to the separation of the

casts; it resembled a coarse, exaggerated crepitation of pneumonia. The temperature varied from subnormal to 100° F.; the pulse was rapid, especially during the paroxysms; sleep was disturbed by the cough and soreness across the middle of the chest. No recurrence took place for some years following and her health was quite restored.

Diagnosis.—In typical cases there is no difficulty; the casts by themselves leave no room for doubt. From *asthma* there may be much difficulty in diagnosis, and in all doubtful cases the sputum should be carefully searched for pellets and masses of rolled-up casts. A *foreign body* in a bronchus may cause similar attacks, but the history and relapses of fibrinous bronchitis will prevent error. *Diphtheria* is to be excluded by the bacteriology and the absence of membrane in the fauces and of laryngeal symptoms. In *pneumonia* casts may occur, but the history and physical signs usually leave no room for doubt. In *bronchitis* the occurrence of dyspnoea and the absence of respiratory sounds over an area of lung, with but slight impairment of the percussion note, might be considered sufficient for a diagnosis, but to make it certain the sputum should be carefully searched for casts.

Prognosis.—A fatal result is rare in an uncomplicated case. In Fagge's case the loosened cast became lodged at the tracheal bifurcation and caused death. In the rare form in which acute attacks follow one another in rapid succession, death may occur during a paroxysm, usually within one or two weeks from the onset. Extensive deposits in the bronchi doubtless occur in such cases. The marked tendency to recurrence is to be borne in mind. The intervals between attacks may be short or long, and liability to them may continue for many years.

Treatment.—The value of any treatment in a disease that runs such an uncertain course as fibrinous bronchitis is difficult to estimate, as any relief following recourse to it may be the natural course of the disease, uninfluenced by the treatment. As there are no known means of preventing the formation of the membranous casts, all that can be done is to give relief as far as possible. If serious symptoms arise from obstruction due to the casts, they should be removed through the bronchoscope without delay. If this measure is not available an emetic may be given in the hope of effecting their expulsion. Potassium iodide is the only drug regarded as of material value by English and American writers. It should be given in full doses.

FETID OR PUTRID BRONCHITIS (GANGRENOUS BRONCHITIS)

Fetid or putrid bronchitis is a rare affection. It is not a definite disease, but only a peculiar form of decomposition which may occur in the secretion in any disease of the lungs or bronchi; it may be a passing phenomenon in any form of chronic bronchitis.

Etiology.—Fetid bronchitis is always a secondary affection which only develops in bronchi previously altered by *acute* or *chronic bronchitis*, *bronchiectasis*, *chronic tuberculosis*, or by *foreign bodies* in the bronchi. It is probable that the organisms which cause the putrefaction are able to develop only on mucous membrane whose epithelium has been injured

or destroyed. Those most liable to the affection are those whose vitality is depressed by privation, alcoholism, and malnutrition. The definite microorganisms that give rise to the decomposition have not been determined; many are found in the secretion and probably several may be able under varying conditions to cause it.

The *Oidium albicans* has apparently been the cause in some cases, the decomposition following exposure to thrush infection. Cases are reported in which *Leptothrix pulmonalis* and *Bacterium termo* have been found in abundance in the secretion. *Bacillus coli* is said by some to be the usual microbe of gangrenous bronchitis.

Pathology.—The morbid changes are few and not constant. The medium-sized and small bronchi are chiefly affected. The diseased bronchial wall is reddish, wine-colored, or pale gray. The epithelium is cast off, and on scraping the surface with a scalpel a soft, fetid pulp is exposed. In many places the wall of the bronchus is destroyed and the process extends to the peribronchial tissue; it may lead to the formation of actual gangrenous cavities. Thus putrid bronchitis is not only an almost constant complication, but also a frequent cause of bronchial dilatation.

The process may terminate (1) in complete recovery or in bronchiectasis; (2) in fatal chronic septicemia or in abscess of the brain; (3) in extensive gangrene of the lung.

Symptoms.—The characteristic symptom is the horrible, gangrenous odor of the patient's breath and sputum; it often permeates the room and even the whole house. The sputum is remarkable for its abundance, especially if there is bronchiectasis, amounting in many cases to several ounces in twenty-four hours. It is muco-purulent and ordinarily separates into three layers. The *upper layer* forms the greater part of the sputum; it is frothy and greenish. It consists of mucus, holding in its meshes many pus and epithelial cells. The upper part contains many air bubbles, and from the lower surface many brownish flakes hang down into the fluid below. The *second layer* consists of dirty, greenish, thin fluid, incorrectly called serum. The *third layer* is formed of sediment of various kinds: detritus, fat drops, and peculiar, horribly offensive pellets known as Dittrich's plugs. These plugs vary in size from a microscopic point up to a bean; they contain fat needles, leptothrix, leucin, tyrosin, and fine granules from degenerated cells.

Cough is frequent, but not severe, as the sputum is brought up with ease. *Fever* is present in many cases, and, being septic, is a serious symptom. It is probably due to the absorption of putrefactive products.

The disease usually begins rather suddenly and is essentially paroxysmal. In strong persons it may disappear after one or many weeks, leaving the patient uninjured. It occurs not infrequently. In severer cases septic symptoms rapidly develop, often beginning with chills. Signs of prostration soon follow, and the patient passes into a typhoid state. Cough and expectoration cease and death in collapse follows.

In some cases complications occur, such as ulceration and gangrene of the lung, and bronchopneumonia, with diffuse bronchitis. In others, metastatic fetid abscesses form in various organs. The disease presents

a very varied history, and the descriptions of the earlier writers varied according to the kind of cases seen. Thus Trousseau describes a relatively mild class, while Traube, Sée, and Andral give the details of cases of great severity which were usually rapidly fatal.

Diagnosis.—The difficulty consists in excluding other affections giving rise to fetid expectoration. It is usually an easy matter to exclude the condition in which the fetor is due to disease above the larynx. When the cause lies below the larynx, however, it may be impossible to be certain that the fetid discharge does not come from bronchiectasis, a gangrenous cavity in the lung, or a gangrenous abscess in the mediastinum or elsewhere in the thorax. In fact, a putrid bronchitis apart from one of these conditions is very rare, so rare that its existence has been questioned, although a few cases, with autopsy, have been reported. It is scarcely possible, however, in any case to exclude bronchiectasis with certainty.

In *gangrene* of the lung, the onset is more sudden, hemoptysis is usually of frequent recurrence, and shreds of pulmonary tissue will probably be found in the sputum; elastic fibres are not often found, as they are rapidly dissolved in the gangrenous fluid.

Fetid expectoration may result from the rupture into a bronchus of an empyema, of an abscess of the vertebræ, the lung itself, or the liver; or of a subdiaphragmatic abscess due to appendicitis or other abdominal disease. In all these conditions symptoms usually develop suddenly without preceding bronchitis, and the source of the pus may be evident on examination. On the other hand, a diagnosis is often impossible; even a postmortem examination may leave it in doubt.

Treatment.—To maintain the best possible general condition and correct the fetor usually sums up the utmost that can be done. For the former, pure outdoor air is of the first importance; then rest or exercise such as each case requires, sufficient nourishment, and the necessary tonic and stimulating remedies accomplish all that we are able to do for the general health. For the fetor, inhalations of antiseptic vapors are usually the most effective remedies. The best deodorant is probably creosote given by inhalation. Inhalations of turpentine are often useful. Both remedies may be given internally. West regards musk, a grain in a pill, or an equivalent of the tincture as the most efficacious remedy. Intratracheal injections of antiseptic remedies should be effective. Auto-genous vaccines should be of much benefit.

BRONCHIECTASIS

Etiology.—Bronchiectasis occurs partly as the result of an increased pressure acting on the bronchial wall, and partly as the result of a change in the texture and condition of the bronchial wall, as well as the surrounding lung tissue. The bronchi are always infected early, pneumococci and influenza bacilli probably being the most frequent infecting organisms. The infection gradually invades the whole thickness of the wall of the bronchi and peribronchial tissue. The diseased condition of the bronchi renders them less resistant to pressure, and therefore the more easily dilated by internal pressure or external traction.

As to the physical cause by which bronchial dilatation is produced there has long been much uncertainty. An important contribution to the problem was made by the investigations on the pneumonia complicating influenza, by Opie, Fauman, Blake, Small and Rivers.¹ They found that "bronchiectasis is most conspicuous in the basal part of the lower lobes and is usually more advanced on the left side than the right. Small bronchi, with no cartilage in their walls, may reach a diameter of 0.5 cm. More advanced bronchiectasis has been found in several necropsies performed late in the outbreak."

Klotz (personal communication) describes the details of three similar cases of bronchiectasis. The first patient, a young man, was stricken with acute influenza with severe tracheo-bronchitis and bronchopneumonia; he died on the eighth day. Necropsy showed the usual conditions in such cases: acute pleurisy and acute confluent bronchopneumonia affecting many areas in both lungs; the bronchi and bronchioles, intensely congested and dilated, could be easily laid open and their ramifications traced to the borders of the lung; the bronchioles were irregularly dilated, some of them with pouches like small aneurisms, others diffuse and cylindrical, the walls of the bronchioles could be recognized around each sac. Microscopic study showed a marked inflammatory process infiltrating not only the surrounding structures but also the walls of the bronchioles, their muscular coat showing marked degeneration. From the contents of the bronchioles numerous influenza bacilli were isolated in pure culture.

The second patient was a laborer in a chemical factory, in which an explosion occurred, setting free irritant gas that caused great respiratory distress and acute tracheo-bronchial inflammation followed. A few days later he became dyspnoeic, at first on slight exertion, later continuously so with cough and expectoration. He had the symptoms and signs of acute bronchopneumonia. Death occurred on the twenty-third day following the accident. Necropsy showed evidences of recent fibrosis, general bronchopneumonia, in some parts in small areas, in others in large confluent masses. Scattered through both lungs, the bronchi showed irregular dilatations, which on a cross section of the lung gave a honey-comb appearance. In the most marked fibrosing areas the bronchi and their branches on being laid open longitudinally were found dilated, in many places to several times their normal diameter. These tubes showed partial desquamation of their epithelium and considerable degeneration of the muscular coat.

The third patient a student, aged twenty years, had a mild coryza and bronchitis. A week later there was shortness of breath during a long walk. He was comfortable during comparative rest during several days following. Three days before his death he had some dyspnoea and general mucous rales, tubular breathing and dyspnoea were found but no fever. The dyspnoea increased and cyanosis appeared. Death took place four weeks after the onset of his illness. At necropsy, wide-spread areas of fibrosing bronchopneumonia and an interstitial pneumonia, also irregular fusiform dilatation of the bronchioles, some to four or five times their normal

¹ *Jour. Am. Med. Assn.*, 1919, **72**, 536.

calibre, with partial desquamation of the epithelium were found. Only a few localized pouches were found. In the lower lobes, the bronchioles were most extensively affected. Later it was learned that the illness had been measles and the character of the interstitial pneumonia made this probable.

These three cases showed identical changes—fibrosing bronchopneumonia, degeneration of the muscular coat of the bronchi, desquamation of epithelium and dilatation of the bronchi. Each was due to a special cause—influenza, infection following “gassing,” and measles. The destructive action of the gas in the second case may have had a part, in addition to infection, in causing the dilation. They all indicate that acute bronchiectasis of the bronchi and bronchioles has its origin in injury of the muscle fibres which surround them.

These reports seem to put on a firm basis both the cause and physics of bronchiectasis. The causes resolve themselves into two groups: First, those having their origin in disease of the bronchi, and second, those due to traction on bronchi by progressive fibrosing pneumonia.

The disease of the bronchi causes degeneration of the muscular fibres, followed by loss of tonicity and elasticity resulting from these changes. The dilatation follows these changes and arises from a variety of causes, such as inertia of the diseased area due to loss of tonicity and elasticity, possibly the most important factor; constant traction by the normal parts of the lung, increased on inspiration; increased pressure caused by cough and strain; accumulation of material in the cavity and wider extension of the disease in the lung. The existence of dilated tubes and the small pouches along their walls indicates that pressure of the air within the tubes was greater than the external pressure effective through the diseased inert tissue of variable density surrounding the tubes.

The increase in the size of the cavities may arise from advancing ulceration in their walls or from traction of progressive fibrosis in the surrounding lung, more often by both causes. That pulmonary fibrosis may cause bronchiectasis is well known. The fact was well demonstrated in some soldiers who had been severely “gassed” and apparently recovered, remaining well for a year or more, then rather suddenly becoming ill with symptoms of respiratory distress, some fever and prostration. If death followed the necropsy showed that there had been a mild, slowly progressive interstitial pulmonary inflammation with many bronchiectatic cavities in which there were only slight change in the tubes and little secretion. These cavities were doubtless due to irregular traction by the slowly progressive interstitial fibrosis of the lungs and the pleural adhesions that so frequently existed.

Bronchiectasis is not rare in children, usually following whooping cough and measles, and probably influenza and other forms of bronchitis. The symptoms and signs are similar to those in adult cases. As in the adult, the outlook depends on the depth of the bronchial lesions, but as tissue reproduction in children is highly active they doubtless recover from lesions which, in the adult, would persist and often become worse.

Morbid Anatomy.—There are two chief kinds of dilatation—*cylindrical* and *saccular*. The *cylindrical* is usually fusiform but may show many

PLATE I



Bronchiectasis. (Carswell.)

irregularities due to the contraction of bands of fibrous tissue in the walls of the cavity, which usually contains thick, altered pus and débris, frequently very offensive. The adjacent lung tissue may be healthy but is more often œdematous, condensed, or fibrosed. These changes may affect a great area of the lung which may be dense and indurated. In many cases the pleura is also affected, sometimes acutely with effusion; more frequently there are irregular adhesions, often with much thickening from which areas dense fibrous bands may extend into the lung toward, and even to the hilum. However, in cases with chronic bronchiectasis, especially if confined to one lobe, there may be no demonstrable change clinically in the adjacent lung tissue.

The *saccular* form may occur in great numbers in a large mass of lung in which the pulmonary structure has disappeared, or less numerous and smaller, embedded in normal lung tissue. They form usually in the terminal bronchi and may be of only microscopic size. They may be of congenital origin.

Symptoms.—Paroxysmal cough and copious, purulent expectoration, often offensive, are the chief features of bronchiectasis and without which a diagnosis is not possible. They occur most commonly on rising in the morning and on lying down at night; that is, change of position, if the cavities are full, causes dislodgment of secretion, and this excites the cough and expectoration. The dilated, diseased bronchi have lost their normal sensibility to such a degree that contact of secretion does not excite cough, and it is not until the accumulated secretion is brought into contact with the more healthy mucous membrane that cough results, usually with the expectoration of large quantities of purulent secretion, as much as 25 to 30 ounces (700 to 900 cc.) in twenty-four hours.

The *sputum* is chiefly purulent; it is usually yellowish and has little adhesiveness. The stagnant, bronchial secretion becomes early infected by organisms including those which cause putrid decomposition. Both the breath and the sputum of the patients usually become offensive, often extremely so. After standing some hours the sputum usually settles into two or, more often, three layers; the lowest one of thick, purulent material containing various kinds of granular débris, and forming an opaque, gray mass; over this a thin, turbid fluid; and if there is a third one, an upper, thin, frothy, brownish layer. In the lower, dense layer there are to be found pus cells, granular detritus, many organisms, and Traube's or Dittrich's plugs, which consist of fetid, soft, grayish-yellow bodies formed in the smaller bronchi from the pus, detritus, crystals, etc. Blood in the sputum is a late, but not infrequent, symptom. It is generally small in quantity and mixed with the secretion; but the bleeding may be profuse and repeated; it may even be fatal.

Fever may be absent throughout but in most cases the course is marked from time to time by exacerbations of two or three weeks' duration, during which there are irregular elevation of temperature, increase of cough and expectoration, sweats, loss of appetite, etc. These attacks are probably due to fresh infections of the bronchi, the occurrence of new areas of bronchopneumonia, and to absorption from the decomposing bronchial

secretion. In cases with marked venous stasis from cardiac weakness the temperature is, as a rule, subnormal.

Clubbing of the fingers is frequent and important as a sign of bronchiectasis. The toes may be similarly affected. In more advanced cases similar changes may occur also in the other phalanges, in the metacarpal bones, in the bones of the wrist and forearm, leg, etc., until finally all the changes of pulmonary osteo-arthritis are present.

Lardaceous or amyloid changes are prone to occur late in the disease, diarrhoea and albuminuria are then often met with.

Physical Signs.—Bronchiectasis may be secondary to such a great number of diseases, and such a variety of morbid changes may develop in its course, that there may be the greatest variation in the physical signs. The signs are those of the associated conditions rather than of the bronchial dilatation. The chest may be enlarged and emphysematous, or, from fibrosis of the lung, it may be markedly retracted, and the heart displaced. The percussion note will vary according to the degree of dilatation, its proximity to the surface, the condition of the surrounding pulmonary tissue, and the thickness of the overlying pleura. If a large dilatation is near the surface, the percussion note will be dull while the cavity is full of secretion, but will become tympanitic as the secretion is expelled and the cavity fills with air. Normal resonance immediately surrounding the seat of a cavity differentiates a dilatation from a tuberculous cavity, as the note is always dull in the vicinity of the latter. A cavity stationary in size points to bronchiectasis, while, as Stokes pointed out, an increasing excavation is preceded by consolidation and is peculiar to tuberculosis.

Auscultation.—In bronchiectasis with emphysema the respiratory sounds are vesicular with a tubular quality, but not cavernous. The sounds may be wavy, both in inspiration and expiration. When there is fibrosis around the dilatation, which is usual in the sacular variety, the vesicular breathing is lost and the sounds are definitely cavernous, usually with more or less “gurgling.” Bronchophony and pectoriloquy may be marked. Adventitious sounds are present in great variety. In the absence of fibrosis there are soft rales, both large and small; if the lung is indurated they are higher pitched and crackling, or, more usually, coarse and metallic. They appear and disappear as the secretion increases or lessens. Associated bronchial and pulmonary diseases produce a variety of rales which may obscure the signs of dilatation.

Complications.—The cause of death is often a complication. Severe hemoptysis, acute pneumonia, and bronchopneumonia are the most frequent. Gangrene of the lung in the neighborhood of the dilatation may occur and lead to a fatal termination. The diagnosis of such a complication is very difficult, as the odor and appearance of the sputum are similar in both affections. If, on microscopic examination, masses of pulmonary tissue are found, the existence of gangrene would be established. A bronchiectatic cavity near the surface of the lung may rupture into the pleural cavity which was not obliterated by adhesion; empyema or pyopneumothorax will follow, and either is usually fatal.

Pyemia is of frequent occurrence. In mild cases it may cause general

malaise, with aching pains; in more severe infection various local infections may occur, such as abscess of the liver or kidneys, suppuration of joints, ulcerative endocarditis, and septic infection of the serous cavities. The most frequent of these metastatic infections is *in the brain*, causing *abscess*.

In many cases death results from cardiac failure due partly to general weakness, but chiefly to obstruction to the pulmonary circulation caused by the fibrosis of the lungs.

Diagnosis.—This depends almost wholly on the expectoration of a large quantity of gray offensive material consisting of pus, granular debris and liquid, but little if any mucus, as the mucous membrane is largely if not wholly destroyed. The expectoration at first is slight but increases until it becomes copious and offensive owing to the invasion of many microorganisms, some of which cause fetid decomposition. The history may extend over months or even years. After the expectoration of a large quantity of secretion, cavernous breathing may, in some cases, be heard over the position of a cavity, to disappear with its refilling. The perforation of a local empyema into the lung might give rise to similar signs, especially if it is situated between the lung and diaphragm, or in an interlobar fissure. In one patient a local empyema arose from an appendix abscess burrowing behind the anterior abdominal wall, over the liver, and perforating the diaphragm. A localized empyema resulted and perforated the lung. The purulent sputum was abundant and very offensive.

Emphysema and chronic bronchitis may offer some difficulty, but the sputum is seldom so copious and fetid; yet in "putrid bronchitis" there is fetor even in the absence of dilated tubes. In a circumscribed gangrene of a lung there is fetor but the expectoration contains much dark blood and shreds of lung tissue.

Prognosis.—In cases resulting from measles, whooping cough, or influenza in children, recovery is frequent, if the dilatation is moderate. In the adult complete recovery is rare, but less severe cases may live an active life for many years, forty or more. In patients in whom the disease follows changes in the bronchi, the duration is longer than in those following fibrosis of the lung. In "gassed" and influenza cases in adults the outlook is grave, as in many of them a masked progressive interstitial pneumonia exists, which may prove rapidly fatal.

Treatment.—As our efforts to cure the dilatations are seldom effectual, we are restricted to the necessity of endeavoring to lessen the secretion and to keeping it as nearly aseptic as possible. The best means of accomplishing these objects is to have the patient live in a pure air which aids also in improving the general health. The greatest care must be taken to prevent inflammatory processes of any kind, even the slightest infection of the respiratory tract. In the attempt to render the secretion aseptic, use has long been made of inhalations of creosote, turpentine, phenol, menthol, etc., vaporized in fairly hot water. Success has resulted from the continuous inhalation of coal-tar creosote vapor and the intralaryngeal injections of solutions of menthol, guaiacol or iodoform, in olive oil, aided by the "postural method" for emptying the cavities. In the absence of any contraindication, the patient should make systematic

efforts at stated intervals to empty the cavities by assuming such positions as lying over the side of the bed with the head down nearly to the floor, to favor the discharge of secretion by gravity. By emptying the cavity he is relieved, to a certain extent, of toxic effects, and the cavity is the better prepared for disinfection by the vapor or fluid that may be used.

The protracted inhalation of creosote vapor has been used to excite sufficient coughing to force out secretion from the bronchi, and to secure efficient disinfection by the prolonged inhalation of the vapor. The vapor should be used in a small air-tight room or tent in the centre of which a small flat dish is fixed on a tripod with a lighted spirit lamp under it; creosote, 15 or 20 drops, is put in the dish; the fumes are inhaled. Later, stronger fumes can be inhaled and greater heat may be applied so as to fill the room with dense fumes. As the vapor is irritant to the eyes and nose, they require to be protected by covering the eyes with watch-glasses framed in adhesive plaster, and plugging the nostrils with clean cotton. With such protection the patient can tolerate an inhalation with comparative ease that could not otherwise be endured. At first, from a few minutes to one-half hour is sufficiently long for an inhalation; later, it may be borne for one to two hours.

The inhalation excites violent paroxysms of coughing and causes the expulsion of large quantities of secretion, even although much has been expelled just before the inhalation began. This residual secretion is usually horribly offensive from having lain long in the cavities. The sputum, at first profuse and fetid, becomes, in favorable cases, gradually lessened in quantity and the odor diminishes; in four or five weeks the quantity may be trifling and the odor slight. The respiratory capacity is also increased so that much greater exertion can be undertaken without dyspnoea. The patient's general condition grows better in every way; the temperature, if elevated, gradually becomes normal, and the pulse stronger. This treatment must be continued for several months but unfortunately is not uniformly successful. The inhalation of creosote from a nebulizer, operated by compressed air, should be equally effective and would be less disagreeable and more easily managed.

Treatment by intratracheal injections has sometimes given satisfactory results. The following may be used: menthol, 10 parts, guaiacol 2 parts and olive oil 88 parts. A teaspoonful of this is injected twice daily, care being taken to introduce the tip of the nozzle of the syringe beyond the vocal cords. This fluid may prove irritating and cause severe coughing. If the tongue of the patient is well protruded and held outside the mouth, and at the same time swallowing is refrained from, the liquid projected against the wall of the pharynx runs down into the air passages. The vapor of this fluid has an effect similar to the creosote fumes.

A dry climate, free from sudden changes, is most suitable for patients with profuse secretion. For the more robust the bracing, dry air of a northern climate, such as the Canadian Northwest, should be very beneficial; the debilitated will do better in a milder climate, such as that of Southern California, where they can spend many hours out-of-doors without much exertion or difficulty in keeping warm.

In a case reported by R. D. Rudolf with well-defined signs, high irregular fever, copious sputum and loss of weight, after failure by other means, artificial pneumothorax was induced but with difficulty as there were many pleural adhesions. For a few days there was increase of expectoration but it soon lessened; the temperature fell, sweating ceased, the general condition improved and weight increased.

Surgical means may succeed if there is only a single cavity definitely located, and the pleural cavity obliterated over the part affected. Bronchoscopic drainage is of great value even in chronic cases in relieving the symptoms. It should be employed as soon as the diagnosis is made and in early cases offers some hope of cure.

CONGENITAL BRONCHIECTASIS

Congenital bronchiectasis is probably more common than is supposed, at all events, it is not a rarity, as might be proved if necropsies on infants were more frequent. "*Bronchiectasis due to imperfect or mal-development of the bronchi*" might be a more suggestive title as indicating the cause and development. The rarity with which traces of alveolar tissue have been found in the affected lung is embryological evidence of the failure of the bronchi to form the alveolar structures. This failure may possibly depend on an atelectasis or be caused by defective development of the lung and hypertrophy of the bronchial mucous membrane, from which bronchiectatic cavities of various sizes develop usually before birth, but sometimes after. It seems possible, if not probable, that the cases in which there are many *saccular* cavities in a lobe of the lung in adults, often with marked atelectasis, are congenital in origin. The bronchiectatic cavities may attain a large size. In a case reported by Koeckert¹ the lower lobe and remains of the upper lobe of the left lung were atelectatic, and the upper lobe almost wholly replaced by an enormous cyst filling the greater part of the chest cavity. The child cried normally at birth but was slightly cyanotic and otherwise appeared quite normal. An hour later there was marked dyspnoea and cyanosis; death occurred one-half hour later. At necropsy there was slight emphysema in the right lung and the right ventricle was slightly hypertrophied. In the left lung the alveoli were collapsed. All the epithelium found was of bronchial origin.

There is considerable literature on the subject, chiefly German and French. The first reported case was by Herman Myer.² The condition varies in degree from a small area to most extensive involvement which causes death of the fetus. Of those surviving after birth, some reach puberty and even adult life. Neiser³ reported the case of a man aged forty years, with persistent symptoms of bronchitis from early childhood, and without a history of influenza, whooping cough or measles. The left lung from the fourth rib in the axilla and the angle of the scapula downward was dull. His son, aged nine years, had signs of a similar

¹ *Am. Jour. Dis. Children*, 1919, **17**, 95.

² *Virchow's Archiv.*, 1859, **16**, 78.

³ *Ztschr. f. klin. Med.*, 1901, **42**, 58.

condition in the corresponding part of his left lung. The roentgen-ray films in both cases were in accordance with the probable diagnosis. While the lesion usually affects a whole lobe, it may be confined to a part of it. Bronchitic symptoms begin in early childhood and persist without remissions. If bronchitis from usual causes occurs it will probably extend to the abnormal part of the lung which doubtless possesses lowered resistance.

In most instances, the *diagnosis* must be uncertain. Its probability may be based on the facts, that the symptoms began in early childhood, have persisted, and that the known causes of bronchiectasis—whooping cough, measles, or influenza—had not occurred before the symptoms began. The existence of cyanosis, even of slightest degree, is an important sign. It is due to the anoxemic blood from the atelectatic part of the lung.

STENOSIS OF THE TRACHEA AND BRONCHI

Etiology.—Narrowing of a bronchus may occur in a great variety of acute and chronic affections. The cause may be situated without or within the tube, or in the bronchial wall itself.

Intrabronchial Causes.—(1) Foreign bodies and (2) tumors or diseased glands which grow into or perforate a bronchus.

Extrabronchial Causes.—(1) Pressure from diseased and enlarged bronchial glands. The lymphatic glands lie chiefly at the lower end of the trachea and around the main bronchi, the largest being at the bifurcation. Tuberculosis is the source of infection of the glands in the great majority of cases. In children the lymphatic glands are normally large and very active, and therefore very liable to become infected, so that the bronchial glands may be greatly diseased, although the lungs are little, if at all, affected.

Constriction of the bronchi is occasionally caused by the pressure of an inflammatory mass resulting from periadenitis. The contraction of the cicatricial tissue produced may also compress the bronchus. In the latter case there may be stridor, contraction of the chest walls, weakened respiration, and dulness. In slowly developing cases the stridor and dyspnoea may be absent.

2. *Aneurisms* of the second part of the arch of the aorta are those most likely to press on the air tubes. They usually develop upward and backward and press on the trachea at its bifurcation. As the chest is shortest in all its diameters at the upper part, even small aneurisms may produce marked pressure. Bronchostenosis may be the only indication of the condition until hemorrhage occurs. Similar symptoms may arise when the aneurism is of the innominate or the left carotid artery. Aneurism of the descending aorta may extend forward and compress the left bronchus.

3. *Mediastinal Tumor.*—The malignant forms are the most important, as by their continued growth they are certain, sooner or later, to press on the bronchial tubes. It is not, however, by pressure on the air tubes alone that they produce their symptoms. Dyspnoea may be caused by secondary deposits in the lungs, pressure upon large vessels, pleuritic effusion, bronchitis, and pneumonia, and by laryngeal spasm excited by pressure on nerves.

The *diagnosis* may be easy if the signs of a solid mass in the mediastinum are definite, such as dulness beneath and on each side of the sternum and in the interscapular region. If the lung tissue over the mass is not completely airless there may be increased vocal fremitus and resonance with tubular breathing; fulness of the veins of the chest or of the neck, with, in many cases, oedema of the corresponding parts owing to pressure caused by obstruction to the return of the blood to the heart; pressure on arteries, as shown by a small pulse; pressure on the laryngeal nerves, causing paralysis or spasm of the laryngeal muscles; and pressure on bronchi, obstructing the entrance of air into the lung.

4. *Abscess* in the mediastinum may be indistinguishable from tumor. It may arise from disease of the bronchial glands, sternum, vertebral column, clavicles, or oesophagus.

5. *Syphilitic infection* may involve the bronchial glands. In Hodgkin's disease and leukemia the bronchial glands are frequently affected and often form enormous masses, which may compress the bronchi.

6. *Pericardial effusion and dilatation of the left auricle* occasionally become so great as to compress one or both bronchi. Hypertrophy of the heart may possibly compress the left bronchus and the trachea.

Stenosis due to disease of the bronchial wall itself occurs most frequently in the smaller bronchi. Only those affections in which the stenosis causes the chief symptoms should be considered as cases of bronchostenosis. Among these is a disease first recognized during life by Fränkel, and which he described as *bronchiolitis acuta fibrosa obliterans*. It may be fatal in a fortnight. His attention was drawn to it by Lange's description of the postmortem findings in two cases. The lungs were described as thickly studded with small, white nodules, as in acute miliary tuberculosis, and it was seen that the bronchioles were blocked with new connective tissue. Fränkel's first case was a man who had inhaled caustic vapor in large quantities, and was at once attacked with dyspnoea, which passed off after a time. Repeated attacks of dyspnoea followed. On admission to the hospital there was extreme difficulty in breathing, with cyanosis, and the lungs were greatly increased in volume. No distinct dulness was found, but everywhere small, vesicular sounds were to be heard; there was no fever. There was temporary relief as the acute inflammation following the necrosis of epithelium caused by the gas abated, but the dyspnoea recurred when the granulation tissue in the injured bronchiolar walls increased and narrowed the bronchioles, in many places even closing them.

Other causes of stenosis are:

1. Ulcerations following traumatism, as burns, injuries by foreign bodies, etc.

2. (a) Syphilitic ulceration followed by cicatricial contraction; (b) syphilitic peribronchitis; (c) gummata in the walls of the larger bronchi.

3. Tumors of the bronchi.

4. Perichondritis.

5. *Bronchostenosis ecchondritica*, described by Gerhardt. In a case there was found marked thickening of many cartilaginous rings and covered by a layer of bone.

Pathology.—Besides the constrictions, bronchial dilatations exist above and below the point of constriction, the proximal widening being due to the inspiratory force, and the distal to the expiratory. Emphysema is common. If the obstruction is in a bronchial branch there may be atelectasis of the corresponding portion of the lung.

Symptoms and Diagnosis.—Distinctive symptoms and signs occur only when the cause affects the trachea and larger bronchi. Dyspnoea is the chief symptom, beginning gradually and increasing as the narrowing of the tube increases, being greater with exertion and coughing. If the lesion is in the trachea, its most common seat, it will soon cause increasing dyspnoea, which later may become paroxysmal and alarming, especially when the patient lies down. There is always some cough, due to irritation and to secretion collecting behind the stricture. There is *stridor*, similar to that in laryngeal obstruction, but without movement of the larynx or change of voice, except some weakness of it. In tracheal stricture the head and shoulders are held forward, while in laryngeal obstruction they are held backward. The respiratory sounds are equally weak over both lungs. If the stenosis implicates one bronchus, coarse rales are present, most marked on the side of the constricted bronchus.

When a bronchus is constricted, especially if there is no disease of the trachea, the breath sounds on the corresponding side will be weak and the lung less expanded; the mediastinum, including the heart, will be moved toward the affected side in proportion to the loss of expansion. The apex impulse may be found near the sternum or even into the right side if the right bronchus is the one obstructed; if the left, the impulse may be found in the left axilla.

If one or both bronchial branches are the seat of disease, the symptoms and signs will be similar to those of obstruction by a foreign body, except that they develop gradually, or to any other cause, such as accumulation of secretion beyond the obstruction, spreading local bronchitis, changes in the part of the lung related to the obstructed bronchus, and possibly to bronchiectasis.

Stenosis from Causes Acting within the Trachea and Bronchi.—*Syphilis* is an important cause of stenosis in the trachea and primary bronchi. A *tracheotomy tube*, long retained in position, has caused such a degree of ulceration that stenosis has resulted. In severe attacks of influenza the mucous membrane may be so swollen as to obstruct, even fatally, the trachea and large bronchi. In the use of the bronchoscope, especially by unskilled hands, the mucous membrane is sometimes so much injured, especially in young children, that obstruction results from the swelling of the membrane, especially near the glottis.

Stenosis from external pressure may be caused by an enlarged thyroid gland. The pressure may be applied on the sides as well as the front of the trachea. An enlarged thymus gland may cause similar results. In both cases the trachea may be deflected, if the pressure occurs chiefly on one side, and increase the stenosis. Similar results may arise from the pressure of enlarged lymph nodes, of an aneurism of the innominate or carotid artery or the transverse part of the arch of the aorta, and of an abscess from spinal caries. Disease especially if malignant, of adjacent

organs as the œsophagus and mediastinal glands, may extend to and invade the trachea and large bronchi.

Prognosis and Treatment.—These depend wholly on the nature of the cause. In stenosis from syphilis and pressure by aneurism, large doses of potassium iodide may do much good, and even in cases of uncertain diagnosis the iodide may prove of much service. In the paroxysmal dyspnoea caused by the pressure of an aneurism, inhalation of chloroform, venesection, or hypodermics of morphia and atropine may give relief. In occasional cases of cicatricial stenosis, dilatation of the constriction may be possible.

BRONCHIAL CALCULI (BRONCHOLITHS)

The term *broncho-pulmonary lithiasis* is applied to the occurrence of stony concretions in the respiratory passages and organs. Calculi may be formed in the bronchi, lungs, pleuræ, or lymphatic glands, and may consist of cartilaginous, bony, or calcareous substance. Bronchial lithiasis is usually latent; calculi being frequently unexpectedly found at autopsy, especially in chronic tuberculosis; but calculi may be formed in other diseases and give rise to symptoms that simulate tuberculosis.

Clinically, the affection seldom shows signs of its existence except in the expectoration of calculi; this is rare but was known to ancient writers. Boerhaave described the case of the botanist Vaillant, who expectorated four hundred calculi. In general the number expectorated does not exceed one or two. The “stones” may be cartilaginous, osseous, or calcareous, and the cartilaginous calculi may originate from the tracheal or bronchial cartilages, being set free by ulceration; or from enchondroses of the tracheo-bronchial cartilages of inflammatory origin (Virchow); or from chondromata of the lung. These calculi have the appearance of cartilage and they can only be differentiated by microscopic examination from cartilaginiform masses of fibrous tissue, which may be set free from a tuberculous lung by ulcerative processes.

Osseous calculi may originate from the *bronchial cartilages*, ossification following inflammation of long duration, as in bronchiectasis and pulmonary phthisis; from *pleural ossifications* occurring in old pleurisies; from *pulmonary ossifications* which form in the walls of old abscesses; in tuberculous and non-tuberculous scleroses and in true osteomata, and, very rarely, in the *tracheo-bronchial mucous membrane*, the seat of old disease.

Calcareous stones are due to the calcification of various tissues of the respiratory organs and to the incrustation of exudates by the deposit of granules of tribasic phosphate of lime and carbonate of lime, without any tendency to ossification. The calcifications in the respiratory organs may be parenchymatous or form in cavities.

In the first group are: calcifications of the tracheo-bronchial cartilages, as observed in aged persons; calcifications of tuberculous bronchial glands; calcifications in the lungs, which may be healthy or previously diseased; calcifications of various tumors; calcifications of the pleura following purulent exudates. In the second class: free concretions in

preëxisting cavities and in inflamed dilated bronchi or in pathological cavities of the lung, especially in those of tuberculous origin. These concretions result from the incrustation of stagnant, muco-purulent secretions. They may also be found in the bronchi, around a foreign body of any kind.

FOREIGN BODIES IN THE BRONCHI

This is a much more important subject than is generally recognized. It presents such a variety of signs and symptoms that the space available will only permit of a brief statement being made of them. That the accident is relatively frequent is evident from the great number of cases treated by Chevalier Jackson. The medical aspects of the subject have been discussed by McCrae in his Lumleian Lectures.¹ It is not a matter for wonder that the accident occurs but that it is not more frequent, if we consider the prevalence of the uncleanly habit of holding all sorts of articles in the mouth. This is natural to the child and many adults retain the habit throughout life. With a sudden fright, movement, a cough, sneeze or laugh, the glottis is put off guard and in the inspiration following, the object, even a very large one, may be drawn into the trachea. In dentistry and operations on the throat, the aspiration of a tooth, small instrument, or a piece of tissue, is a well-known accident especially during anesthesia.

Symptoms.—The symptoms vary from the slightest disturbance to those of strangulation. It is of the greatest importance to be alive to the fact that a foreign body, even a large one, may pass through the glottis without being even suspected; the disappearance of a foreign body held in the mouth is usually attributed to its being swallowed. More frequently there has been some choking with severe coughing, usually soon ceasing and leaving no discomfort. This quiescent period is of varying length and when symptoms arise some time later the slight disturbance felt at the time of inspiring the foreign body is often forgotten. Lodging in the trachea it generally causes at least some substernal discomfort, which soon disappears if the object is small and does not move. If it moves with respiration, it may be driven against the glottis and cause severe cough even to the point of strangulation, with loud, long, croupy inspirations. Gradual relief follows as the irritability of the mucous membrane lessens leaving only substernal soreness and often some impediment to breathing. If the body moves or passes into a bronchus, cough and distress recur. If secretion is abundant it will pass into the bronchi on both sides and cause coarse rales over both lungs. Lodging in the bronchus and not moved by respiration there may be no symptoms for an indefinite time; if it is light and moved by the air it will cause cough and may be shifted into another bronchus. When fixed, local inflammation results and the secretion may excite cough and expectoration. Vegetable bodies excite the most severe inflammation, peanuts being the most active irritants. The foreign body may completely obstruct the bronchus. Before doing so, it may be moved about by respiration and cough,

¹ *Lancet*, 1924, i, 735, 787, 838.

injuring several bronchi. Swelling of the mucous membrane from the irritation and infection may cause complete closure of the bronchus. In the very young, the reaction is most severe and may be quickly fatal.

On entering a bronchus, the body usually passes down until arrested by one too narrow for entrance and lodges there. If it is smooth and irregular it offers only partial impediment to the entrance of air; when regular it may completely block the tube and put out of commission the related portion of lung which collapses as soon as the residual air is absorbed. Collapse of a small portion of lung will cause no conscious disturbance; even when large there may be no discomfort at rest, but on exertion, shortness of breath will be in proportion to the amount of lung rendered inactive. If the foreign body is moved slightly by the greater force of inspiration some air may enter and none escape in expiration, and thus lead to greater resonance or even tympany on percussion, the respiratory sounds and tactile fremitus remaining little if at all altered.

Much depends on the nature of the foreign body. If it is inorganic, as a safety-pin or tack, local inflammatory changes will be slow in developing—such as swelling and granulations of the mucous membrane. Secretion, at first around and below the obstacle, may later extend upward even to the trachea. Often there are quiescent periods. The body may be shifted to another bronchus, even to the other lung, the signs also shifting. Organic bodies such as pieces of food, nuts, corn, etc., rapidly excite broncho-pulmonary symptoms, especially when a peanut is the offending body. The condition may simulate pneumonia, empyema or tuberculosis.

A small body may at once descend until arrested in a small bronchus where it will cause little if any cough or discomfort as the irritability in small tubes is slight. This symptomless interval may last an indefinite time, even months. Inflammation of the bronchus follows and the secretion fills the distal portion of the bronchus. It becomes purulent and some of it may force its way past the obstruction and some air may enter restoring some degree of resonance and allowing more expansion of the chest and descent of the diaphragm. The degree of these changes varies with the size of the bronchus and the continuance of air entrance. The inflammation in the bronchus may lead to the destruction of its wall and disease of the adjacent lung tissue with resulting bronchiectasis. In the meantime, inflammation of the tube extends toward the trachea, and infection may extend to other lobes or even to the opposite lung.

During this time constitutional symptoms may vary from negligible ones to the very severe. If the body is metallic, the general disturbance is usually moderate, but if a nut or other organic substance, the illness may be very grave, with high fever, rapid respiration and pulse, severe cough and abundant and often offensive sputum. Many of these latter may prove rapidly fatal unless the body is promptly removed.

The *physical signs* may be readily interpreted, or be as uncertain as the symptoms. The "asthmatoïd wheeze" is an important sign if present. It occurs when a bronchus is partially obstructed. The lung in which the foreign body lies is indicated by lessened expansion on that side. Auscultation usually gives important results. If the foreign body remains fixed

then the signs may be stationary, but not necessarily, as the secretion often invades other bronchi and causes signs to appear in other parts, it may be in the other lung, giving the condition much more the appearance of tuberculosis.

If a bronchial tube is obstructed, in the part of the lung related to it, the respiratory sounds are weak if the obstruction is partial, but if complete the breath sounds disappear and the percussion note soon becomes flat as the air is quickly absorbed. If the body acts as a "ball valve," permitting air to enter but none to escape, the affected part of the lung will be distended and the chest also; the percussion note is highly resonant or tympanitic, but there are no respiratory or voice sounds. If the body is shifted to another bronchus, the signs shift with it, the former seat, if not greatly damaged, in a short time becoming normal.

If the obstructing body is shifted to the other lung, there may be a quiescent period, the damage in the lung first concerned rapidly improving. The signs later appear in the second lung, and cause a repetition of signs and symptoms. As the signs are subject to such rapid changes, examination should be repeated frequently.

After a thorough investigation has been completed, roentgen-ray examination, if available, should be resorted to in all suspected cases. If efficient, it rarely fails to indicate the presence and position of the foreign body, even if it is a vegetable substance which does not show in the plate; the changes in the lung are evident but require skilled interpretation.

Diagnosis.—It is of the first importance to remember that a foreign body, even a large one, may have entered the respiratory tract without any history to indicate such an accident, especially in children. If it is in the respiratory tract a diligent investigation will find it. The roentgen-ray study, if thoroughly efficient, offers great assistance.

Treatment.—There should be no unnecessary delay in removing the foreign body. If the body is in the trachea and moves with respiration, tracheotomy is usually the safest course if a skilled bronchoscopist is not available. If the sides of the opening in the trachea are at once held widely apart, the cough, that nearly always follows immediately, drives the body out through it. In case of severe symptoms this course seems advisable as otherwise a sharp cough may force the body into the glottis, where it may become impacted, with a fatal result.

Treatment has become vastly more successful with the advent of the bronchoscope; if not too long delayed and in competent hands the failures have almost reached the vanishing point. Owing to the danger of subglottic œdema in children after bronchoscopy a constant watch should be maintained in order that tracheotomy may be done promptly if dangerous symptoms are manifested. If much damage has been done by the foreign body careful treatment is called for. Even in severe cases recovery is usually rapid after the foreign body is removed.

HEMORRHAGIC BRONCHITIS OF NON-TUBERCULOUS ORIGIN

Hemorrhagic bronchitis may be caused by a great variety of parasites, animal and vegetable, the latter being much the most common but the

former the most wide-spread. They all prevail much most frequently in tropical countries, but, as the world has grown much smaller owing to the great facilities for travel, many patients migrate, but some have been found who were infected in temperate climates. A full but brief and excellent statement of the subject in general was given by Castellani¹ at the International Conference on Health Problems in Tropical America, held at Kingston, Jamaica, in 1924. To it the writer is much indebted for information on the subject.

The cause of the disease may be one or more of a great variety of parasites of animal and vegetable origin. Those thus far discovered and investigated, may be best indicated by the following classification suggested by Castellani.

- | | |
|---|--|
| A. Due to animal parasites (1) Protozoa
(Broncho-zoiases) (2) Metazoa | { 1. Broncho-spirochætosis
2. Broncho-amœbiasis
Broncho-paragonomiasis |
| B. Due to vegetal parasites } (1) Fungi imperfecti
(Broncho-mycosis) | { 1. Broncho-nocardiasis
Synonyms:
Broncho-streptothricosis
Broncho-cohnissstreptothri-
cosis
Broncho-actinomycosis
Broncho-discomycetosis
2. Broncho-anaeromycosis
3. Broncho-moniliasis
4. Broncho-cryptococcosis
5. Broncho-hemisporosis
6. Broncho-sporotrichosis |
| (2) Ascomycetes | { 1. Broncho-saccharomycosis
2. Broncho-endomycosis
3. Broncho-oidiosis
4. Broncho-aspergillois
5. Broncho-penicilliosis
6. Broncho-acremoniellasis
7. Broncho-cladosporiosis
8. Broncho-accladiosis
9. Broncho-sporotrichosis |
| (3) Phycomycetes | Broncho-mucocormycosis |

Broncho-spirochætosis.—The *Spirochata bronchialis* was first described by Castellani in 1905. His first cases in Ceylon sought advice on account of recurrent hemoptysis. Repeated examinations of the sputum were made and no tubercle bacilli found, but there was an enormous number of spirochetes, especially in the blood portions of the expectoration, and virtually no other organisms. Later he found many other cases. Within a few years, his work was confirmed by investigators in various tropical countries. Since then the disease has been found in both Europe and America. Chill often acts as an important predisposing cause. That the disease is spread by infection by the spray from coughing is at least possible. It may be also that some persons have quiescent spirochetes in the bronchi and that increase of the activity of the organisms probably occurs as in ordinary bronchitis after a chill.

¹ Proceedings of the International Conference on Health Problems in Tropical Countries, 1924. Published by the United Fruit Company, Boston, Mass.

Symptoms.—The disease may be acute, mild or chronic. In the *acute* form the onset may be sudden, with chilly sensations, general pains, and moderate fever, the latter lasting from two to twelve days. The cough is severe and the sputum scanty, muco-purulent and at times with traces of blood. The general condition is usually not affected but in some prostration is marked. In both acute and mild cases auscultation may reveal no signs but there may be a few slightly dull patches with crepitation in the lungs but no leukocytosis. The occurrence of dull areas indicates that the organism may enter the blood and through it infect the lungs. The *chronic* form may follow single or repeated attacks of the acute or mild forms, or the onset may be gradual. There is always cough, often severe, in the morning. Definite hemoptysis may occur. Fever may be absent, or present and hectic in character; it may occur in the morning and be absent in the afternoon. Coarse rales are often the only common sign; some however show small areas of consolidation. The general condition may remain good for long periods, although some anemia may exist, and a few patients show wasting. In some cases there may be a large quantity of purulent expectoration, sometimes bloody, and at times high intermittent fever. In another group there are the signs of chronic bronchitis with asthmatic attacks.

Diagnosis.—This is based on microscopic examination of fresh sputum with dark-ground illumination; the material may be stained with the Romanowsky stain or with silver nitrate methods. *Spirochetes* are found in great numbers; bacteria are few or absent. *Acute* cases are differentiated from influenza and malaria, which they resemble, by the examination of the sputum and the occurrence of blood in the sputum. The *subacute* or *chronic* group, if there is blood in the sputum, is usually regarded as tuberculous; the absence of bacilli excludes the latter. The prognosis is favorable as to life, but the disease may run a very chronic course, with wasting and anemia.

It is to be noted that spirochetes are to be found in *pyorrhœa alveolaris*. They are found at times in diseased tonsils and in tracheo-bronchitis, probably as saprophytic organisms. Vincent and others regard the spirochetes as identical with the organism in Vincent's angina; Chevalier Jackson found the Vincent's organisms in a local bronchitis caused by a foreign body. In the secretion in this case there were large flakes of membrane.

Treatment.—For *acute* cases, rest in bed, acetyl salicylic acid in small doses, and codeine and tartar emetic, of each gr. $\frac{1}{6}$ to $\frac{1}{4}$ (0.011 to 0.016 gm.) usually suffice. In the *subacute* and *chronic*, tartar emetic gr. $\frac{1}{6}$ to $\frac{1}{4}$ (0.11 to 0.016 gm.) and liq. arsenicalis, m 2 to 3 (0.13 to 0.3 cc.) are usually effective; potassium iodide may aid. In severe cases with high fever, neoarsphenamine intravenously in the usual doses, is often efficacious.

Broncho-amœbiasis.—This form of bronchitis, occasionally with hemorrhage, is met with in *amœbic hepatitis*. Cases without hepatitis or dysentery are also reported. The bronchitis is rather severe, the expectoration muco-purulent, stained with blood, and occasionally with free hemoptysis. Amœbæ are found in the sputum. Emetine is specific.

Broncho-mycoses.—There is a large variety of these fungi, any one of which may be found in the sputum of bronchitis. The symptoms may be mild with the sputum muco-purulent and containing the fungi. In severe cases the symptoms are those of grave pulmonary tuberculosis, with fever and hemorrhagic expectoration. Mild cases may recover spontaneously; the administration of potassium iodide benefits some. The *prognosis* varies with the character of the fungus, the *Nocardia* group causing the gravest outlook.

Broncho-streptothricosis.—This is one of the most severe forms and is generally chronic. Most patients are, or have been, in tropical climates but some have been infected in temperate climates. The fungus grows in long slender filaments that show true branching. It is met with in temperate climates but occurs more frequently in the tropics. Infecting the bronchi it causes inflammation that may result in bronchiectasis. The features are fever, anemia and loss of flesh. The expectoration is muco-purulent and tinged with blood; free hemorrhage occurs in some cases. There may be signs of focal lung infection, patches of dulness, crepitation and pleural friction. In the sputum segments of branching fungi are found but no tubercle bacilli. Iodide of potassium internally and auto-genous vaccines give good results in some cases, but many are not improved and end fatally.

Broncho-actinomycosis.—This form occurs in northern climates as a bronchitis in which there is cough with blood-tinged sputum containing small granules formed by great numbers of thin mycelial filaments with débris. *Treatment* with potassium iodide in large doses gives fairly good results in some cases if continued until all traces of the disease are eradicated, otherwise, if a focus is left, it will develop and a recurrence follow, usually ending fatally. It is often difficult to prevail on the patient to continue treatment after the symptoms and signs disappear.

Broncho-moniliasis.—This has been met with not only in tropical and subtropical countries, but cases are also reported from various parts of Europe and America. There is a great variety in this fungus and its effects. *Clinically* the results of infection vary from the mildest, causing no general symptoms, to the most grave. The expectoration is muco-purulent, usually scanty, and contains no blood. In the chest there are no signs, or, at most, only a few rales. The symptoms may disappear spontaneously after many weeks; or a severe form may develop with symptoms like those of tuberculosis, emaciation, fever and expectoration with hemorrhage. In the chest patches of dulness, etc., may be found. The termination may be fatal.

The tea experts and factory employees in Ceylon are subject to a “*tea cough*,” due apparently to the inhalation of the *monilia fungus* which is found constantly in tea dust.

In *treatment*, iodide of potassium is effective in some but fails in others. Vaccines may be useful. Creosote in addition to the iodide is recommended.

Broncho-aspergillosis.—The fungi are usually only saprophytic, but may become true parasites and cause extensive damage especially to the lungs. They are widely distributed and may be found in vegetables

and grains. Infection may occur by inhalation of the spores. The symptoms are those of bronchitis with muco-purulent expectoration and usually fever. In severe cases, hemoptysis may occur. These are often fatal, and at autopsy nodules may be found in the lungs, liver and other organs. Occurring as a secondary infection, it has been long known to be present in bronchitis, bronchiectasis, bronchopneumonia, pulmonary gangrene, carcinoma and, probably more frequently, in pulmonary tuberculosis. The *diagnosis* depends on a thorough examination of the sputum. The *treatment* is not promising. In early cases potassium iodide may prove effective and creosote inhalations have been advised. Removal to pure air in a moderate climate and care as in pulmonary tuberculosis are advisable.

These are only a few, the more important, of the parasitic infections of the bronchi, so far known. An important point is that their symptoms closely resemble those of pulmonary tuberculosis and the cases are nearly always diagnosed as such. Roentgen-ray examinations have always been regarded as indicating a tuberculous infection and the results have been accepted as final. Unfortunately, examination of the sputum in suspected cases of tuberculosis is so generally confined to a search for tubercle bacilli that the possibility of the presence of other organisms is not considered. "X-ray diagnosis" is an unfortunate term and has led to many errors which could be avoided if the clinical examination was complete and thorough.

It will be noted that there is no report with reference to the pathological changes in the bronchi in any of the cases. In many of the diseases the lungs are also affected, there being signs of small areas of consolidation with rales and pleural friction; the infection probably being blood borne. Some of these were fatal and came to necropsy; even in these no report has been made as to the condition of the bronchi. Such a report would settle the doubt that has been raised as to the bronchitis being a disease entity. The literature on "The Hemorrhagic Bronchitides" is large and growing rapidly. It offers remarkably interesting and instructive information.

CHAPTER VI

DISEASES OF THE LUNGS

By HOBART AMORY HARE, M.D.

CIRCULATORY DISTURBANCES OF THE LUNGS

Congestion of the Lungs.—Etiology and Pathology.—As commonly employed, two quite different circulatory disturbances of the lung are included under the term congestion, which is therefore subdivided into the active and the passive types.

1. *Active Congestion* (hyperemia of some writers).—In this condition an increased amount of arterial blood is thrown into the lung and consequently it is found in the initial stage of all inflammatory diseases of the lung and pleura, as pneumonia, bronchitis, tuberculosis, and pleurisy. During the cold stage of the paroxysms in malaria and in other diseases accompanied by rigors, an excess of blood is distributed to the lungs. The inhalation of excessively hot or cold air or irritating gases brings about the same state, at times very rapidly fatal. Violent exertion excites active congestion, and athletes have died apparently from this cause alone. Affections of the pons or medulla are possible excitants of the condition, and it may precede the fatal termination of coronary artery disease. A zone of hyperemic tissue surrounds essentially every circumscribed lesion of the lung, whether pneumonia, tuberculosis, abscess, gangrene, or new growth. That active congestion is ever a primary lesion, instead of a symptomatic affection, is extremely doubtful, although many French writers vigorously support this view. In cases of pure active congestion the morbid anatomy and histology are essentially those found in the initial stage of lobar pneumonia.

2. *Passive Congestion*.—This is practically always due to faulty action of the heart, which may depend upon a weak right ventricle or upon obstructive or regurgitant lesions in the left side. To these as causes may be added non-aëration of the lung and compression or thrombosis of the pulmonary veins. Two important types of the condition are observed: (a) brown induration and (b) hypostatic congestion.

(a) *Brown induration*, also called mechanical congestion, accompanies lesions of the left heart which prevent the proper outflow of blood from the lungs. Histologically, the vessels of the lung are distended. The pulmonary connective and elastic tissues increase in amount. In the slowed blood of the distended veins, actual stasis appearing in some areas, increased hemolysis occurs, and pigment from the disintegrated red cells is deposited in the interstitial tissue and in the alveolar epithelium. Chronic bronchitis also ensues. The increased pulmonary and bronchial tissue causes induration; the pigment gives to the organ a brown color. When incised surfaces are exposed to the air they become

bright red from oxidation of the excessive amount of hemoglobin. The sputum contains leukocytes and pigment-bearing cells which have become detached from the alveolar walls. From the nature of the affection primarily responsible for their appearance, the latter are by some writers called "heart-disease" cells.

(b) *Hypostatic congestion* is that form determined by gravity in addition to slowed pulmonary circulation dependent upon weak cardiac action and deficient aëration. It is not uncommon in prolonged febrile diseases, as typhoid fever, and in adynamic states in general. For the latter reason the aged are particularly prone to the affection. Prolonged recumbent posture for any cause favors this form of congestion. It has followed morphia poisoning and is particularly apt to occur in persons suffering from brain lesions, notably those which induce paralysis or coma. The posterior portions of the lungs, or the outer portion of one lung if the patient has lain on that side, are dark in color, heavy, pit on pressure, and on incision drip blood or bloody serum. The vessels in the alveolar walls are distended and the perivascular tissues contain an excess of serum. Under these conditions the serum and less often some blood passes into the vesicles, the air is thereby expelled, and the part sinks when placed in water. To this condition the terms *hypostatic pneumonia* and splenization have been applied, the latter possibly being appropriate only when considerable blood is in the vesicles. The alveolar epithelium shows granular degeneration and usually more or less extensive desquamation.

Symptoms.—*Active congestion* of the lungs is characterized by sudden onset, beginning as a rule with a chill and rapidly developing dyspnoea, which is accompanied by sharp pains in the side, cough, and expectoration. The sputum is frothy and contains blood. The temperature may rise to 103° or even higher, but the fever does not persist, falling by crisis on the third or fourth day. Aëration of the lung is diminished, so that cyanosis together with distention of the superficial veins of the neck may be well marked.

The thorax may be somewhat distended and show impairment of resonance. The breath sounds are harsh and rough, and rales of various kinds may be detected; thus at the base of the lungs fine crepitant or subcrepitant rales may be distinctly audible, while over other parts sibilant and sonorous rales may be heard. Vocal fremitus may also be somewhat impaired. In some cases of active hyperemia the pleura is considerably involved, so that a friction rub is heard. A slight exudate may also take place. To this form Potain gave the name of pleuro-pulmonary congestion.

It is evident, therefore, that primary active congestion developing after exposure to cold or injury is, at the beginning of its evolution, not unlike genuine pneumonia.

The symptoms of *passive congestion* consist in slight shortness of breath upon exertion, and a hard, usually dry cough, which has a tendency to increase upon the slightest provocation. Expectoration varies; at times it may be slight or absent, and again it may be of moderate degree. In the latter instance the sputum frequently contains blood. Attacks of

hemoptysis may also occur. The vesicular murmur may be diminished and moist rales be plainly heard over the base of the lungs. If the cardiac lesion is mitral, symptoms of pulmonary oedema may appear.

The symptoms of *hypostatic congestion* are not definite. As hypostasis develops very slowly in many cases, nothing but slight acceleration of respiration may be present for some time; but when its evolution is more rapid, as for instance in the acute infectious diseases, a pronounced degree of dyspnoea together with cyanosis may appear with comparative suddenness. As soon as exudation occurs and the fluid gravitates, increased fremitus, dulness, and moist and crepitant rales will be found. The vesicular murmur also is diminished or absent.

Diagnosis.—In regard to active congestion, it is evident that the affection possesses no distinctive characteristics. In the beginning it may resemble pulmonary infarction or genuine pneumonia, but as it progresses it will be readily distinguished from both these diseases. From infarction it is differentiated by the disappearance of bloody expectoration and subsidence of other symptoms within a much shorter period than in the former disease. Absence of hepatization and the occurrence of crisis on the fourth or fifth day distinguishes it from lobar pneumonia. The initial chill is said to be less violent than in pneumonia. Primary congestion of the lungs differs from bronchopneumonia both in the manner of onset and evolution, and these differences constitute a means for differential diagnosis. The diagnosis of passive congestion will be made easy by the discovery of the causative cardiac lesion.

Difficulty of breathing and cyanosis developing during the course of an adynamic disease should always arouse suspicion of hypostatic congestion, particularly if no elevation of temperature occurs in association with the other symptoms. From pleural effusion developing in the course of such an affection or in bronchopneumonia, hypostatic congestion can be differentiated by the fact that in effusion the level of dulness changes when the patient changes his posture; and the percussion note is duller than it is in hypostatic congestion.

Prognosis.—In *active hyperemia* the prognosis is usually favorable, but in some cases oedema may develop with fatal result, or pneumonia be superimposed upon the congestive process, thereby rendering the prognosis less favorable. A few cases following a sudden chill, which resulted from exposure to cold when the patient was in an overheated condition, have been reported as terminating fatally within a few hours. As a rule, however, the symptoms subside within a few days and complete recovery results. Nevertheless, the affection is always to be looked upon as serious, and one demanding active treatment. The prognosis of *passive congestion* depends largely upon the condition of the heart, which is responsible. In some patients an insidious nephritis is a predisposing cause.

In *hypostatic congestion* the prognosis varies with the condition in which it develops, with the vitality of the patient, and the promptness with which the pulmonary involvement is discovered and treated. In old and feeble persons the disease is almost invariably fatal, and in young children the mortality is also very high.

Treatment.—In active congestion prompt measures must be taken to arrest the hyperemic process. For this purpose cups should be applied posteriorly or a large mustard plaster applied. If marked cyanosis is present venesection may be resorted to with good results. Concentrated liquid nourishment must be provided. The dietary mentioned in the article on Bronchopneumonia is appropriate.

In the treatment of passive congestion measures directed to the causative cardiac affection will most favorably influence the pulmonary condition. Full doses of digitalis with efficient doses of strychnine will do good service. A small dose of codeine may be useful in allaying the chronic cough. Intercurrent attacks of acute bronchitis are to be treated in the usual manner.

As concerns hypostatic congestion, prophylaxis is quite as important as treatment. Aged or feeble persons confined to bed should not be allowed to stay in one position, but should be made to assume a different posture every hour or two. Whisky or brandy is often useful in maintaining circulatory equilibrium. The slightest manifestation of bronchitis in such persons should immediately lead to the institution of treatment. When the disease has once developed the primary indication is to support the heart, and for this purpose digitalis should be given. Atropine sulphate is also of value. Digitalis should be given every four hours, ℥ 30 (2.0 cc.) of the tincture being administered until its effect becomes apparent and the frequency of its administration being reduced in accordance with the indications of the individual case. Dry cups should be applied over the base of the lungs posteriorly. Active purgation may do good if the patient's strength permits it. In nearly all cases a brisk mercurial purge will do no harm and may do good.

Œdema of the Lungs.—**Etiology.**—Localized, collateral, or focal œdema occurs in the tissue surrounding circumscribed lesions of the lung, as inflammatory areas, new growths, abscesses, infarcts, and tuberculosis, being congestive and in some instances toxic or inflammatory in origin. *General œdema*, either acute or chronic, is not so readily explained. In the chronic form it accompanies chronic pulmonary congestion, chronic nephritis, cachexia, anemia, cerebral disease, and chronic infections. In cases of slowly oncoming death it may occur as the so-called terminal œdema. Regarding this type, Coplin's statistics indicate that too large a percentage of cases has been attributed to this relatively unimportant cause, with the result that an undeservedly lessened significance has become attached to pulmonary œdema as a whole. In 2030 autopsies, most of them upon persons dead of chronic diseases, œdema was found in but 405, or 20 per cent., leaving 80 per cent. of deaths unaccompanied by noticeable accumulation of serum in the lungs. Disease of the heart is the most frequently preceding lesion, that organ being affected in 350 of Coplin's 405 cases.

Acute pulmonary œdema occurs particularly in connection with diseases of the kidneys or arteries, although other predisposing causes are alcoholism, extreme cold, and intense mental emotion particularly in old people. It not rarely complicates uremia and eclampsia, and is the final phase of an apoplexy. Of practical interest is the œdema following

anesthesia, particularly that induced by ether, and the form developing with various infectious diseases, as typhoid fever, pneumonia, and influenza, this being in favor of the belief that the condition is toxic in origin. This view has been ably upheld by French writers, while most German observers prefer the mechanical theory as an explanation. The classic experiments of Welch led him to believe that pulmonary œdema is due to increased capillary tension, produced by an excess of blood from the right heart over that handled by the partially disabled left ventricle. This is a plausible explanation in some cases, especially the terminal œdemas. Welch himself now speaks of the frequency with which bacteria, apparently in colonizing numbers, are found in œdematous lungs. The acute pulmonary œdema produced experimentally by the injection of epinephrine very closely simulates that in human beings, but in its development mechanical and toxic effects are possibly combined, and hence this cannot be regarded as a type of the condition due purely to circulatory disturbance. The most acceptable view as to the etiology of pulmonary œdema is that it is due to increased capillary tension accompanied, aided, and probably in many instances preceded, by degenerative changes, toxic in character, of the capillary endothelium.

Morbid Anatomy.—The base of the lung posteriorly is chiefly affected, but the entire organ may be involved. The œdematous lung is heavy, boggy to the touch, and pale in color, unless darkened by associated congestion, which is frequently present. It pits on pressure and is readily incised. From the incision flows an abundance of frothy serum. At first this is almost clear, but later, especially if pressure upon the lung be made, it becomes blood-stained; the degree of congestion determines the prominence of this feature. The bronchi contain frothy fluid which may be blood-stained. Crepitation is always lessened but is often present throughout the organ; small patches may be airless. These if excised will sink in water, but they are commonly so small that care in excision is necessary to prevent expression of the fluid. Careful pressure on larger areas will expel the fluid and thus differentiate them from patches of actual consolidation due to inflammatory conditions. Occasionally the affected areas are gelatinoid in consistency, due to partial and probably postmortem coagulation of the œdema fluid; in them, however, fibrin is never abundant.

Microscopically the bloodvessels may be distended, although usually this is not conspicuous and often is entirely absent. The fibrils of the connective tissue are widely separated by the distended lymph spaces. In the alveoli are few or many leukocytes, variable in type, and a small quantity of residual granular material from the serum. Fibrin may be present, but never in large quantities. Red blood cells are usually scanty except in acute fulminating œdema, when they are commonly numerous. This accounts for the conspicuous reddish color of the frothy fluid which is often expectorated in extraordinary quantities in these cases. Slight catarrhal bronchitis may be manifest. In the bronchial walls and peribronchial structures, including the lymph nodes, the presence of an excessive amount of serum is evident.

Symptoms.—These consist in rapidly developing dyspnœa, cough, and expectoration. Breathing is very difficult and becomes progressively worse as the exudate continues to accumulate. The patient is anxious and terrified and is fully conscious of the danger which threatens him. As the œdema increases the pulse becomes weak and small, cyanosis changes to lividity, a cold sweat breaks out over the body, the extremities become icy, consciousness is lost, and death ensues with the manifestations of profound asthenia. The temperature is usually subnormal.

In cases of very rapid evolution, a class to which French clinicians have applied the term *hyperacute œdema*, a fatal termination may occur within a few minutes after the onset of symptoms. The manifestations of œdema of the lung occurring as the terminal event of exhausting diseases are usually not so violent as those just described, the onset and evolution being more gradual, and the symptoms less pronounced. Expectoration is usually profuse and contains a high percentage of albumin; it is often frothy and of a pink or red color.

The *physical signs* are not characteristic. Upon percussion normal resonance is diminished, particularly over the posterior portion of the lungs. Occasionally small patches of tympany may be found interspersed throughout the dull areas. Upon auscultation various rales—fine and coarse, mucous, bubbling, and crepitant—are heard.

Diagnosis.—An adequate history together with the symptoms and physical signs in the majority of cases suffices to make the diagnosis clear. Acute œdema might be mistaken for pulmonary embolism, which also has a sudden onset marked by severe dyspnœa. The difference in the character of the sputum and the not uncommon absence of physical signs, or the difference in their character when present, distinguish the latter affection. In uremia the results of the urine examination and the possible presence of Cheyne-Stokes breathing afford a means of differential diagnosis. Although the symptoms of hydrothorax are in some respects similar to those of œdema of the lung, the physical signs are different; dulness is more pronounced and its limits vary with the posture the patient assumes. The hyperacute cases may be confounded with cardiac paralysis or angina pectoris, and postmortem examination be required to disclose the cause of death. If the physician sees the patient while alive the nature of the trouble may be determined.

Prognosis.—This depends upon the underlying causative affection. It is always grave, no matter upon what condition it may depend.

Treatment.—This must be directed both to the immediate source of danger to life—that is, to the œdema, and to the causative affection. For the first purpose, counterirritation in the form of dry cups or a large mustard plaster should always be employed, and in the more urgent acute cases venesection may be used with advantage provided there is venous engorgement. When cups are used they should be applied over the entire posterior pulmonary area. Inhalations of oxygen may be tried in the hope that they will allay dyspnœa. The heart must be stimulated by camphor and ether administered hypodermically. Atropine is *facile princeps* in the treatment of this condition. It is the writer's

practice to give gr. $\frac{1}{50}$ (0.0012 gm.) hypodermically for the first dose and then use a smaller quantity at the end of one hour if indications for its employment are still present. Strychnine and caffeine should be freely given hypodermically.

Hemoptysis.—**Etiology.**—The term *hemoptysis* should be limited strictly to the phenomenon of blood-spitting, but is by common consent interpreted as meaning the ejection of blood in any quantity coming from the respiratory tract. The numerous causes include:

1. *Pulmonary tuberculosis*, which is by far the most frequent single cause of hemorrhage from the lungs. Usually, the blood comes from eroded vessels which may lie in the walls of cavities, but less advanced disease may cause the symptom. Occasionally, the walls of small vessels infiltrated by the tuberculous process, instead of becoming thrombosed, as they usually do, rupture and give rise to hemorrhage. From this source the quantity of blood is commonly sufficient only to color the sputum, but small quantities of almost pure blood may be expectorated. Stress is placed by some writers upon aneurismal dilatation of vessels in the tuberculous areas as predisposing to rupture and consequently to hemorrhage. While this change undoubtedly occurs its great frequency is not indicated by autopsy findings.

2. *Ulcerative lesions* of the larynx, trachea, or bronchi. These usually lead to slight hemorrhage only, but in some cases a vessel of size sufficient to cause serious or fatal loss of blood is eroded. Fibrinous bronchitis may give rise to profuse hemorrhage when the cast is expectorated.

3. *Chronic lesions of the heart*, especially mitral stenosis, not infrequently give rise to hemoptysis which may occur at intervals for years. The quantity of blood is commonly small.

4. In the initial stage of various *inflammatory* lesions, as lobar pneumonia, the sputum is often blood-tinged.

5. *Abscess* or *gangrene* of the lung.

6. *Trauma* in the shape of blows upon the chest, or falls, or wounds of the bronchi or lung by foreign bodies aspirated or penetrating from without; under the last is to be included puncture by broken ribs.

7. *Syphilis*, *leprosy* and *actinomycosis* are among the rarer causes.

8. *Malignant growths* of the lungs or air passages. Ulceration of the tumor may be the direct cause, but intrapulmonary growths may produce it by virtue of the surrounding hyperemia.

9. *Emphysema* is an unusual cause, unless there be marked bronchiectasis. When occurring, the amount of blood is commonly small, but the condition has proved fatal.

10. *Recurring hemoptysis* in subjects of chronic arthritis has been observed.

11. *Pulmonary hemorrhage* has followed heavy lifting.

12. *Bronchiectasis* is occasionally complicated by hemorrhage.

13. Diseases accompanied by hemorrhages elsewhere, or by hemorrhagic tendencies, as scurvy, leukemia, and purpura, may cause troublesome bleeding from the lungs.

14. Hemorrhagic *infarct* of the lung may give rise to hemoptysis.

15. In cases of arrested menstruation, the lung may be the seat of vicarious hemorrhage without showing a definite lesion. This is certainly very rare.

16. Ware called attention to pulmonary hemorrhage in young persons who are healthy so far as diagnostic methods are able to determine and who do not afterward suffer from tuberculosis. Of 386 persons exhibiting pulmonary hemorrhage, 62 recovered from that affection and did not later show tuberculous lesions.

17. *Hysteria* in some instances appears responsible for pulmonary hemorrhage. The case recorded by Pende is unique. A rugged girl, aged seventeen years, developed recurring hemoptysis subsequent to the death of a sister from pulmonary tuberculosis. Stigmata of hysteria were present and signs of pulmonary lesion were absent. The hemoptysis was for a time controlled by suggestion, but finally proved fatal. Autopsy revealed no lesion of the lungs. One doubts the value of this record.

18. *Aneurisms* of pulmonary or neighboring vessels rupturing into the lungs. Among these are the aorta, pulmonary artery, innominate, carotid, and even the subclavian and bronchial arteries. The hemorrhage may be relatively slight if from a small vessel or the partially thrombosed contents of an aneurismal sac of a large artery, or it may be rapidly fatal if a large sac ruptures.

19. Pulmonary *distomatosis*, known from the cause and the symptoms as parasitic or endemic hemoptysis, is due to the presence in the lung and bronchi of the *Paragonimus westermanii*.

20. Not infrequently small quantities of blood, enough to stain the saliva, arise from rupture of varicose vessels in the soft palate or pharyngeal mucous membrane.

Symptoms.—The circumstances under which hemoptysis occurs, as well as the physical signs associated with it, vary with its cause. The bleeding may be very slight or profuse. Thus when it develops as an initial manifestation of tuberculosis it is often slight, in bronchiectasis it is usually of moderate degree, in advanced tuberculosis and rupture of an aneurism it is copious.

As a rule it is sudden in onset, the mouth all at once becoming filled with blood. Persons who have already had attacks, however, may experience prodromal symptoms which warn them of the impending hemorrhage. They have a sense of tightness and constriction in the chest, some difficulty of breathing and a general sense of lassitude. Soon a sensation of tickling or pricking in the throat ensues, the patient becomes conscious of a salty taste, and the mouth suddenly becomes filled with blood. During an attack the patient is excited and anxious. Unless he is bleeding profusely or the hemorrhage has continued for some time, the face is flushed and the pulse rapid. This increase of the pulse is no doubt partly due to the mental perturbation which is usually present. When a large quantity of blood has been lost symptoms of asthenia are observed; the pulse is weak, the face blanched, the extremities cold, and syncope may supervene.

The physical signs vary with the cause. They are described under the different maladies with which hemoptysis is associated. Palpation

and percussion ought not to be practised during an attack of pulmonary hemorrhage.

Diagnosis.—After the hemorrhage has ceased the most important matter to be determined is whether the blood comes from the lungs, and if so then to ascertain upon what cause the bleeding depends. The principal condition from which hemoptysis is to be differentiated is *hematemesis*. If the patient be seen during the attack it is comparatively easy to distinguish between the two by the difference in the character of the blood. Small quantities of blood from the lungs are bright red in color, frothy, and of alkaline reaction. If the hemorrhage be copious the associated symptoms and the history make the nature of the trouble plain. No reliance is to be placed upon the accounts of the patient or his friends in regard to the character of the attack and the quantity of blood lost. It is not rare to be assured that the patient “bled about a quart,” whereas the nurse could prove that only a few ounces were lost.

In regard to the *cause* of the bleeding, a careful history, with the physical examination, are of the utmost value. Thus if a first attack has been preceded by cough, night-sweats, and loss of flesh the presumption that tuberculosis is the underlying cause is probable. In like manner the discovery of cardiac trouble may explain the origin of certain mild cases. In slight cases of blood-spitting the nose and pharynx should always be examined, as the causative lesion may thus be found. Detection of spurious hemoptysis depends upon the physician’s acumen and knowledge. Blood-spitting in a neurotic or hysterical woman is always suspicious and should put the physician on the alert.

Prognosis.—This depends entirely upon the underlying cause. Although patients are always apprehensive of death during an attack of pulmonary hemorrhage it is very rare for early attacks to terminate fatally. Out of 386 cases observed by the late Dr. Ware, of Boston, only 3 resulted in death during early attacks. Of course, death may take place at once if an aneurism ruptures or a large vessel becomes eroded. So, too, if blood accumulates in a large cavity respiration may be seriously impeded, pneumonia develop, and death result within a few days. In advanced tuberculosis repeated hemorrhages or long-continued moderate bleeding may so weaken the patient as to cause his death.

In marked contrast to these unfavorable effects of hemoptysis are the results of moderate or slight hemorrhage in cardiac disease. Not only do they do no harm, but they frequently afford relief. It has been my experience that moderate hemorrhage in early tuberculosis if not immediately followed by a pneumonia is not indicative of a grave result. Possibly this is because it alarms the patient sufficiently to make him lead a healthy life.

Treatment.—This depends upon the causative factors. In all cases *rest* is of primary importance. If the patient is bleeding and frightened much good will be accomplished if the physician will first of all allay his fears by assuring him that in all probability the attack is not dangerous. Mental excitement and bodily restlessness will thus be overcome. A hypodermic injection of gr. $\frac{1}{4}$ (0.016 gm.) of morphine should be given at once in cases of any severity. It not only quiets the patient, but also

allays the cough and thereby prevents fresh attacks of bleeding. Nitro-glycerine (gr. $\frac{1}{100}$, 0.0006 gm.) should be given hypodermically and repeated in an hour if the bleeding continues. Pieces of ice may also be swallowed. When a suitable apparatus is at hand the great value of artificial pneumothorax is always to be borne in mind. It is of little value if pleural adhesions are present. In patients who have had one or more slight hemorrhages, indicating that a large one may occur, a roentgen-ray examination should be made and recorded so that the usefulness of pneumothorax may be decided if a large bleeding occurs.

In hemorrhage due to congestion, counterirritation in the form of dry cups will be found useful. Arterial sedatives, such as chloral, aconite, or veratrum viride, may be employed with advantage in certain cases. Ergot and astringents, such as lead acetate and gallic acid, are valueless and should not be used. It is doubtful whether chloride of calcium is of any use. Certainly no one would think of giving it to arrest bleeding from a vessel of any size in another part of the body. When due to cardiac disease no treatment other than that directed to the heart is indicated; this form of hemorrhage is usually beneficial.

Embolism, Thrombosis, and Infarction of the Lung.—**Etiology.**—Hemorrhagic infarction or infiltration of the lung (pulmonary apoplexy) is the result of embolism or thrombosis of a branch or branches of the pulmonary artery; *embolism* is much more frequently the cause. Emboli may arise from any part of the venous system of the body, thrombosis being the usual primary lesion, the veins of the leg and the uterus and para-uterine tissues being the most common sites. Emboli also originate in the right heart, particularly in the auricle, and in the pulmonary artery. Numerous cases of fat embolism following surgical operations or fractures of bone are on record and fragments of tissue, especially the liver, have been found in pulmonary infarcts. Regarding the frequency of pulmonary apoplexy as compared with the general processes of thrombosis and embolism in the body, it is to be remembered that very small emboli lodging in the lung may give rise to no clinical evidence of infarction, and that massive emboli occluding large arteries cause death so quickly that infarction cannot occur. *Thrombosis* in the pulmonary arteries depending on pathological changes in their walls is rare. Aufercht maintained that these changes are due primarily to weakness of the heart resulting from endocarditis, myocarditis, pericarditis, or atheroma of the aorta. Whether or not the sequence of changes is as depicted by him, certain it is that the occurrence of pulmonary infarct is favored by enfeebled circulation and that it is most common in chronic heart disease.

Morbid Anatomy.—In the case of embolism of the large arteries, with sudden death, the lung may show no noteworthy changes other than the occluded vessel. The right lung is most often the seat of infarct unless in one of various possible ways the blood current in the right pulmonary artery is weakened. Infarcts are commonly in the periphery of the lung, the posterior edge at or near the base being a frequent site, but they occur in the interior of the organ. They may be single or multiple and vary in size from 1 to 6 cm. in diameter, although rarely a large part of a lobe is involved. They appear beneath the pleura as

PLATE II



Hemorrhagic Infarct of Lung.

approximately circular, elevated, dark-red, or blackish masses that in consistency are quite solid. On section they are more or less perfectly wedge-shaped, the typical infarcted area forming a cone with the base toward the pleura. In some instances, owing to the abundant collateral circulation, the area is almost globular. At or near the apex of the infarct may often be found the plugged vessel responsible for the lesion. Occasionally careful search fails to reveal such obstruction and in some cases a possible source of emboli is not apparent. These instances are cited in support of the opinion that laceration of bloodvessels may, in the absence of obstructive lesion, cause pulmonary apoplexy, but this view cannot be regarded as established. As a rule, localized pleurisy develops over the affected area and a zone of oedematous lung surrounds the infarct. This zone may be also hyperemic, thus giving to the enclosing band a reddish color as contrasted with the dark hue of the central area. As the infarct ages, the color fades because of disappearance of the blood pigment and small infarcts may return almost to the normal hue. Microscopically the alveolar septa and the vesicles are suffused with blood, the latter accounting for the hemoptysis which so frequently accompanies the process. In cases of fat embolism oil may be detected in the sputa.

The *termination* of the simple infarct consists in the disintegration and removal of the red-blood cells by phagocytosis or absorption, often with resulting pigmentation of the surrounding pulmonary tissue or neighboring lymph nodes. The embolus may undergo resolution, and if the infarct was small the part may become approximately normal; that the circulation is ever perfectly reëstablished is doubtful. Fibrous-tissue formation in the area is usually more or less pronounced, in some cases resulting in the substitution of the normal tissue by an irregularly contracted scar. Cases in which the entire infarct separated from the surrounding healthy tissue have been reported. Abscess or gangrene results if pyogenic or putrefactive organisms respectively gain access to the area. If the embolus is composed of tumor cells, a secondary new growth develops in addition to the changes common to non-infected infarcts. Pulmonary emboli arising from suppurative lesions or new-growths are often so small that little or no hemorrhage follows their lodgment in the lung; abscesses or metastatic tumors may therefore develop without the usual phenomena of infarction.

Symptoms.—These vary with the size of the vessels occluded and with the nature of the embolus or thrombus. When the pulmonary artery or one of its large branches is suddenly clogged, the patient is seized with a sense of suffocation and intense dyspnoea and may die within a few minutes. In other cases an attack of syncope comes on; the patient suddenly experiences a feeling of faintness, utters a cry, falls to the ground, and never regains consciousness.

On the other hand when a smaller branch is occluded the onset and termination are not so violent. Symptoms of asphyxia varying in intensity with the size of the vessel which is obstructed are the cardinal manifestations, but the patient does not succumb at once, life being prolonged for several hours. A person with this form of embolism or thrombosis presents a striking picture. Respiration is intensely labored, the face

is livid, the veins of the neck distended, the nostrils dilated, and the eyeballs protrude. The action of the heart is weak and rapid; as the asphyxia advances a cold sweat may appear, it being often the precursor of death. Convulsions have also preceded death.

In cases in which small bloodvessels are obstructed and infarction results very often the first symptom is pain in the side; this is soon followed by difficulty of respiration and, within a few hours, by cough and expectoration. The sputum is always blood-stained and is very often entirely sanguinolent, the blood and mucus being intimately mixed. This form of expectoration may continue for some hours or for several weeks, but as the infarct undergoes resolution it diminishes in quantity and gradually loses its sanguinolent character. During the course it is not uncommon for attacks of hemoptysis to occur, but as a rule the quantity of blood lost is not large. In many cases the temperature is not disturbed, but in others slight elevations occur; they are usually not of long duration. Infective emboli or thrombi may of course produce suppuration or gangrene, in which case hectic fever may be present. Infection of an infarct may also take place through the air passages and likewise give rise to fever. Pneumonia and pleurisy may develop as complications.

Physical Signs.—In the rapidly fatal cases the physical signs are *nil*. In those cases in which life is prolonged a few hours the breath sounds first become weak and then the signs of congestion and œdema develop, so that large bubbling rales and crepitation may be heard. A systolic murmur is also frequently present. In a case of infarction dulness will be elicited over the diseased area of the lung, but sometimes this may not be present, hyperresonance being found. Upon auscultation it is found that the breath sounds are impaired, or perhaps the vesicular murmur may be entirely absent over a circumscribed area. If an area of considerable size be involved bronchial breathing may be heard. Subcrepitant and crepitant rales can frequently be detected.

Diagnosis.—The cases in which the pulmonary artery or one of its large branches is suddenly occluded must be recognized by the presence of the symptoms described as belonging to this class of cases. When the patient is known to have had phlebitis or endocarditis no doubt need be entertained in regard to the cause of his sudden illness and death. Angina pectoris or an embolism of a coronary vessel may produce somewhat similar symptoms. The difference in the type of respiration will serve to differentiate the affection from laryngeal obstruction due to œdema of the glottis which rarely develops so suddenly. The existence of pulmonary infarct will be made plain by the sudden attack of costal pain and dyspnoea, the expectoration of bloody sputum, and the physical signs which have been enumerated.

Prognosis.—Large emboli usually cause death in the manner previously described, although occasionally obstruction of a vessel of considerable size may be followed by subsidence of symptoms within a few hours. The prognosis of pulmonary infarction cannot be considered unfavorable unless it be due to septic emboli. As a rule, resolution occurs, the symptoms subside, the physical signs disappear, and recovery takes place.

Treatment.—Great care should be taken to prevent the occurrence of embolism and thrombosis. Care should be taken to secure good contraction and involution of the uterus after delivery. In case phlebitis develops, absolute rest with immobilization of the affected part should be secured and proper surgical treatment instituted. Those affected with endocarditis should be enjoined to avoid violent exertion of every kind. Absolute rest is of the utmost importance in treating cases which have actually developed and for this reason when a patient is seen in an attack he should not be disturbed for a thorough examination.

The principal indication is to support the heart, and for this purpose the diffusible stimulants are most appropriate. Camphor and ether may be given hypodermically, and large doses of aromatic spirit of ammonia may be administered internally. If the patient survives a few hours strychnine and caffeine may then be used. If much restlessness is present a dose of morphine may be given, provided that marked cyanosis is not present to contra-indicate its use. If great tension of the right side of the heart is present venesection may afford relief.

As the case progresses rest, nourishing food, and the use of the iodides are the appropriate therapeutic measures.

BRONCHOPNEUMONIA

Etiology.—Under the terms bronchopneumonia, lobular pneumonia, catarrhal pneumonia, and capillary bronchitis is included an affection so varied in cause and, although to a lesser extent, in pathology as to lead to the suggestion that it be called a lesion rather than a disease. If from these titles, however, bronchopneumonia be chosen, and for many reasons it is the preferable term, the name itself is significant and limits the disease to a quite definite process, even though the causes are exceedingly diverse. Bronchopneumonia, then, is an affection of the lung in which the usual sequence of events is that an inflammation of the smaller bronchioles in scattered areas is succeeded by involvement of anatomically related or of contiguous vesicles. In cases of the primary form the lesion in the two situations possibly begins more nearly simultaneously, but even here the pathology indicates that the exudate first appears in the bronchioles. As to mode of origin the disease is of two types, the primary and the secondary.

Primary bronchopneumonia includes about one-third the cases. In Holt's series of 443 cases, 154 were of this type, agreeing with Conner's conclusion that 30 to 35 per cent. of reported instances are primary. This type comes on without previous general disease and as the cause in many instances is the pneumococcus, in this, as in the mode of onset, the affection resembles lobar pneumonia.

Secondary bronchopneumonia is due to many different causes, chief among which are the acute infectious fevers of childhood, particularly measles, whooping cough, diphtheria, and scarlet fever. The age incidence of these diseases determines that this type of bronchopneumonia is chiefly in children below five years of age, although it of course occurs later in life; the latter is especially true of that in typhoid fever, smallpox.

and erysipelas, although these diseases are not nearly so frequently complicated by bronchopneumonia as those of the first group. In addition is a second group caused by the entrance into the lung of foreign materials and known as *aspiration* or *deglutition* pneumonia. This occurs in subjects of all ages. In the first, fluids are drawn into the lung. They may be from the mouth in cases of infection of that cavity or during operations about the mouth or throat under anesthesia. In other instances the material comes from the lung itself in the shape of fluid from bronchiectatic cavities, blood from pulmonary hemorrhage, or pus which finds its way into the larger passages. In the deglutition pneumonia solid particles of food gain entrance to the lung. Either fluid or solid material from tumors in the larynx or oesophagus may thus induce bronchopneumonia. Both the aspiration and deglutition forms of the disease are really due to bacteria which pass into the lung with the other material. Some writers prefer not to class these types with bronchopneumonia, but other than the fact that they occur less often than the primary and the other types of the secondary form and finally develop suppuration there appears no valid reason for their exclusion.

In addition to these fairly definite causes of bronchopneumonia there are a host of less positive, but nevertheless important, predisposing factors which may play a part in all cases and which in some are of great significance. *Age* is an important factor. Young children are particularly the subjects of the disease for the reason that the primary affections causing it, by inducing a bronchitis, are prevalent among children under five years of age. In a second class of age incidence are old persons, the extremes of life being particularly subject to the disease, although for somewhat different reasons. This form of pneumonia is very often the terminal event in aged and feeble persons with chronic disorders, as nephritis, diabetes, and cardiac affections. It also occurs in these subjects as a complication of acute maladies, but most often follows lengthy and debilitating diseases.

Among the general predisposing factors which may underlie bronchopneumonia is cold, damp, changeable weather. The effect of this is well shown by the greater incidence of the disease in the winter and spring months. Unhygienic surroundings, poor food, insufficient clothing, overcrowded and badly ventilated sleeping quarters, all favor the disease. As a consequence it is more frequent among the poorer classes, is common in the subjects of rickets and other types of malnutrition, and may become almost epidemic in foundling homes and similar institutions. Tuberculosis very frequently induces bronchopneumonia.

Possibly in no other disease do lessened powers of resistance of the individual, from whatever cause, play such an important part in determining the inception. This statement is borne out by the wide range of bacteria which under favorable circumstances may serve as exciting agents.

The *bacteriology* of bronchopneumonia forms an unsatisfactory chapter. No specific organism has been isolated. The one most frequently present, alone or associated with other bacteria, is the pneumococcus. In Wollstein's series of 100 cases it was present in 67. It was found in 25 of the

33 cases of primary bronchopneumonia, in 15 of them in pure culture. In the 42 cases of the secondary form in which it was present, it was in pure culture in only 10, thus emphasizing the fact that it is especially active in the primary form of the disease. Wollstein's studies show also that this organism was present in a greater number of those cases in which a large part of one or more lobes was affected as compared with the instances of widely disseminated and smaller foci. Other organisms found in bronchopneumonia are the streptococcus, particularly in those cases following infectious fevers and in aspiration pneumonia, the *Staphylococcus aureus* and *albus*, and Friedländer's bacillus. In some cases the *Bacillus influenzae* alone is found. The influenzal bronchopneumonia has special features discussed elsewhere. In 131 cases of bronchopneumonia found in 220 fatal cases of diphtheria studied by Councilman, Mallory, and Pearce, the diphtheria bacillus was third in the list of bacteria recovered from the lung, being exceeded only by the pneumococcus and the streptococcus. Single infections are the exception, mixed infections the rule. When the disease is due to the tubercle bacillus it is best considered simply as pulmonary tuberculosis. With this wide range in the bacterial content of the affected lungs, bronchopneumonia cannot be grouped with the specific infectious diseases, although the bacterial nature of all cases is certain.

Morbid Anatomy.—The affected lung may be slightly increased in size or at least does not collapse so readily as usual or even not at all. On the surface, more commonly posteriorly and in the lower lobes, are dark or bluish depressed areas, usually scattered and small, although occasionally they may include a large part of a lobe. These discolored patches show particularly well in the non-pigmented lungs of children. Between these atelectatic areas the lung exhibits a moderate degree of compensatory emphysema. If the condition be well advanced, slightly projecting solid areas may also be detected. These commonly are not large and may be so small that on first examination the organ appears to creptitate throughout; careful palpation, however, reveals the small, airless foci, presenting on the surface and scattered through the lung as distinct, although often indifferently defined, nodules. These, although not crepitant, lack the pronounced solidity of the consolidated areas in lobar pneumonia. Over the superficial nodules there is often roughening of the pleura or even a fibrinous exudate, this being more marked in the larger foci. The affected part has a mottled appearance due to scattered and alternating areas of atelectasis, consolidation, and emphysematous distention. Section of the lung exposes surfaces moderately dark red in color, smooth, and bathed with blood or bloody serum or blood-stained mucus. The solidified areas project from the surface to a varying degree, but are never very prominent.

A transverse section of such an area shows the affected bronchus filled with grayish mucus and surrounded by vesicles containing the catarrhal exudate. External to these are the collapsed vesicles of the same or neighboring lobules. Longitudinal section of the pneumonic area shows the racemose arrangement of the bronchus and the infundibula and vesicles filled with the grayish or grayish-yellow, mucoid exudate,

some of which can be expressed from the tissue. In some cases these solidified areas are large enough to be excised without obtaining portions containing air, and they then sink in water. With small, widely disseminated foci this test becomes impossible. The intervening collapsed areas are darker in color, smooth, airless, well-defined as separate patches, or, when small in extent, appearing as indistinctly outlined bands passing irregularly between the solidified areas. The bronchi are always more or less inflamed and the peribronchial lymph nodes are usually swollen.

Morbid Histology.—In the affected bronchi is an exudate largely mucoid in character, but containing desquamated and fatty epithelial cells and leukocytes, the former being especially prominent. The bronchial wall is infiltrated with leukocytes and shows evidence of marked oedema. Longitudinal sections may reveal irregular or saccular dilatations of the smaller tubes. The vesicles terminating or surrounding these bronchi are more or less completely filled with a mucoid and cellular exudate similar to that in the bronchi. Fibrin is rarely found and never in quantities approaching that essentially characteristic of lobar pneumonia. The alveolar and bronchial capillaries are distended, and in the walls of the vesicles are numerous leukocytes, the cellular infiltration of the bronchial and alveolar walls being a conspicuous feature of bronchopneumonia. In many instances the walls of alveoli bordering the solidified areas, and which themselves contain little or no exudate, are occupied by great numbers of leukocytes. In the aspiration and deglutition pneumonias with pus formation, the polynuclear leukocyte predominates and necrotic changes are evident.

The termination in non-fatal cases is usually that of *resolution*. This process rapidly rids the lung of the non-fibrinous exudate, the blood-vessels and lymphatics caring for that part which is not expectorated. Newly formed epithelium replaces that lost in the desquamative process and the leukocytes and serum in the bronchial and alveolar walls are removed, the affected areas becoming essentially normal. *Suppuration* frequently terminates the aspiration and deglutition forms of the disease; it is rarely found in the other types. Gangrene occurs in the same kind of cases as does suppuration, occasionally following the latter process. In some instances the affected areas undergo fibrosis.

Symptoms.—As bronchopneumonia arises from the most diverse causes, and as its clinical course depends not only upon the different morbid processes from which it originates and with which it is associated, but also upon the age and previous state of health of the persons affected, a comprehensive description applicable to all the forms under which it manifests itself would seem well-nigh impossible. Nevertheless, it is possible to give a general description of its more salient features, afterward discussing its special traits as modified by the causative factors, the extent of the pulmonary involvement, and the age of the patient.

The disease as ordinarily met with in *childhood* usually succeeds bronchitis, which in turn often depends upon one of the acute infectious diseases, so that, as a rule, symptoms referable to the respiratory organs dominate the clinical picture. The bronchial inflammation is generally present for some time before the lungs become involved. The *onset*, there-

fore, is not abrupt, but insidious. The temperature ascends gradually, respiration becomes difficult, and the cough grows worse. At the expiration of three or four days, pulmonary involvement has become more pronounced and the constitutional symptoms are considerably accentuated. The patient is very restless and is harassed by dyspnoea and cough. The respirations are short, shallow, and very rapid, varying from fifty to seventy-five or even more per minute. The face may be cyanosed and livid, and well expresses the suffering which the patient experiences for want of air. The alæ nasi dilate with every breath, and all the auxiliary muscles of respiration are called into play in an effort to force more air into the lungs. This difficulty of respiration may vary in intensity at different times of the day, being worse at night or in the morning, or exacerbations may occur at any time if secretion accumulates or if laryngeal spasm occurs. The cough is more or less severe; it is frequent, hard, and painful, and is accompanied by slight expectoration. In young children there is very little or no expectoration, secretion either being absent or swallowed. The sputum is rarely blood-stained, and does not have the rusty appearance of lobar pneumonia.

The *fever* varies in severity, and although it may rise as high as 105° it is usually of moderate degree. Preagonal elevations of temperature are not uncommon; they may reach as high as 108° . Morning remissions are marked, although vacillations may take place at any time during the day or night. The fever falls by lysis, which is protracted over several days.

The *pulse* is very rapid, but its increase in frequency is relatively less than that of the respirations. It is not unusual for it to be as rapid as 140 beats per minute, and it may even become so fast as to be uncountable. The action of the heart become weak and irregular and dilatation of the right side may occur.

Anorexia and thirst are always present, and vomiting and diarrhoea are not uncommon. The latter may be of toxic origin, or depend upon gastric and intestinal irritation resulting from the same causes that produced the pneumonia. Mucus which has been swallowed may also be vomited.

As regards *cutaneous lesions*, it is not uncommon to find the characteristic eruptions of the acute infectious diseases with which bronchopneumonia is associated. The heterogeneous rashes of influenza and diphtheria as well as the typical rash of measles are often encountered. The latter, however, is apt to fade rapidly once the pneumonia is developed. In contradistinction to the regularity with which it appears in lobar pneumonia, herpes labialis is very rare.

Cyanosis has been mentioned. When it is pronounced there is very often an associated coldness and clamminess of the skin. Sweating may also occur early in the disease, but it is of a different character than that occurring in conjunction with marked cyanosis, making the skin warm and moist. For the most part the skin is hot and dry during the early stages, but attacks of sweating sometimes occur.

The *urine* is scanty, high-colored, and contains an abundance of salts. Traces of albumin may be found when the fever is high, and larger quan-

tities when such acute infectious diseases as scarlet fever, diphtheria, or influenza have preceded the pulmonary disease.

Pain is not violent, and indeed may be absent. It is not unusual, however, for the patient to complain of dull and occasional shooting pains over the areas of inflammation.

The above clinical picture represents the common form of secondary bronchopneumonia in childhood. Certain variations from this symptom-complex are determined by the extent of the pulmonary lesions, the causative factors and the age of the patient. If the foci of consolidation be few in number and scattered throughout the lungs, the symptoms will not be so severe as those just depicted; the progress of the disease will be milder, its manifestations more irregular, and sometimes its duration is longer. If, on the other hand, the pulmonary inflammation be massive and constantly advancing, all the symptoms will be intensified. Dyspnoea may become so violent that the patient suffocates. This condition has been called "suffocative catarrh."

When bronchopneumonia supervenes upon whooping cough or tuberculosis, its onset and course are particularly insidious. When it complicates or follows whooping cough its progress may be mild or, on the other hand, in infants speedily cause death. In the moderate cases the child is apathetic and sluggish, refuses food, and gradually loses flesh. Some fever is present but the cough is not pronounced. The physical signs, too, may not be well marked. When complicating measles the temperature ordinarily runs a higher and more constant course than in many other forms.

In *primary* bronchopneumonia, or that developing irrespective of any antecedent bronchitis, the clinical picture is different from the one just drawn. The disease is abrupt in onset and often ushered in by chills, high fever, and severe nervous phenomena. The temperature is maintained at a high level, and falls by crisis or lysis. The pulmonary symptoms are overbalanced by the constitutional disturbances. The duration is shorter than that of the secondary form. Primary bronchopneumonia is more closely related to lobar pneumonia than is the secondary form.

In the aged and infirm the symptoms resulting from disseminated patches of pulmonary consolidation are frequently masked by the manifestations of hypostatic congestion. The development of the disease is not characterized by any pronounced clinical phenomena. Its onset may be slow and insidious. Fever, cough and dyspnoea may all be absent, and the disease first be discovered when physical examination is made. It often happens, too, that the physical signs are not distinct and that proof of the existence of patches of consolidation is first obtained at autopsy. The chronic bronchial catarrh, so frequent in the aged, may extend to the bronchioles and produce an exudate with resulting areas of consolidation, and when this is the case the increased severity of symptoms is often attributed to a mere exacerbation of the bronchial trouble.

Just as the morbid anatomy and symptoms of bronchopneumonia are variable, so likewise is its duration. It may last from a few days to several weeks. In acute suffocative catarrh and capillary bronchitis, and

that form superimposed upon the chronic bronchitis of the aged, the disease may terminate fatally within forty-eight hours. The course of the disseminated lobular form is progressive, although irregular, exacerbations occurring as new areas of consolidation develop. Its average duration may be said to be from two to three weeks. In cachectic, strumous children it may last for many weeks. It is unusual for any form of bronchopneumonia to terminate in less than ten days.

Physical Signs.—From what has been stated it is evident that the physical signs must be variable and inconstant. When only small, isolated, and widely disseminated areas of consolidation exist, percussion will not reveal their presence, and even when considerable consolidation has taken place there may be a sufficient degree of compensatory emphysema to overcome the dulness which otherwise would be elicited. Indeed, a hyperresonant percussion note is very common. It is only when confluence of different consolidated areas takes place, or when the morbid process advances so rapidly as to cause massive consolidation, that marked dulness is detected. It is most common over the bases posteriorly. When this condition is present, retraction of the sternum and lower ribs is frequently observed.

At first auscultation reveals only the signs of bronchitis. Moist and fine subcrepitant rales will be heard over various areas of the thorax, particularly over the bases posteriorly. If there is consolidation of considerable extent, crepitant rales and bronchophony will replace these sounds. The former may, however, be obliterated if the bronchi become filled with secretion. Over the upper anterior and lateral parts of the thorax, impairment of the vesicular murmur, a prolonged expiratory sound and sibilant rales are not uncommon. Very often these different physical signs exist simultaneously in various parts of the thorax, some being present on one side and others on the other; or they may alternate with one another, especially in the protracted forms. They are extremely fugacious and not in proportion with the severity of the subjective symptoms. Whereas lobar pneumonia is usually limited to one lobe or lung, catarrhal pneumonia is generally bilateral.

Complications and Sequelæ.—Bronchopneumonia may cause complications which materially influence its progress and modify its prognosis. Of the immediate complications, pleurisy, abscess, and gangrene of the lung, and pulmonary hemorrhage must be considered. The last is very rare. The pleura is sometimes affected, but the inflammation is usually fibrinous and confined to localized areas, although it may be general. Effusion rarely occurs, but when it does take place it is apt to be purulent. Abscess and gangrene are not common, and the former occurs more frequently than the latter. Often abscesses are minute in size, so that they do not cause serious difficulty. If an abscess ruptures into the pleural cavity, which is exceedingly rare but does happen, pyopneumothorax results.

Both *gangrene* and *abscess* are of more frequent occurrence in those forms of the disease dependent upon acute infections, such as measles, diphtheria, and erysipelas, than in those originating from other causes. Gangrene is often associated with noma, which is to be considered as

an expression of the same infection which produced the pneumonia; it is not improbable, moreover, that the gangrenous process itself is due primarily to the same cause instead of being secondary to other lesions in the lung.

The expectoration of blood-stained sputum has been mentioned; it sometimes happens, especially in suffocative catarrh, that enough blood escapes from the intensely congested pulmonary tissues to constitute a slight hemorrhage. Likewise, where there are confluent or extensive areas of consolidation, small vessels may be eroded and permit the escape of blood. These hemorrhages are not of ill omen.

Cardiac involvements such as endocarditis and pericarditis, as well as otitis media and abscess of the brain, are associated conditions depending upon the same cause as the pneumonia. Convulsions and delirium may occur.

The most important sequel and the one most to be dreaded is tuberculosis. It may affect not only the lungs, but the peritoneum and meninges as well. It must be remembered, however, that bronchopneumonia often develops upon an unsuspected tuberculosis which becomes manifest only as the secondary disease progresses, or is first detected when resolution fails to occur.

Diagnosis.—This may be easy or difficult according to the manner in which the disease manifests itself. Thus it will be readily made when there is a frank expression of the symptoms mentioned as belonging to the usual secondary form as met with in childhood. This is especially true when there is sufficient consolidation to produce bronchial breathing and bronchophony. On the other hand, when the onset and evolution of the disease are particularly insidious, or when it develops during the course of pertussis or tuberculosis, and when it is complicated with chronic nephritis or the cachectic states of the aged, both symptoms and signs may be so ill-defined as to escape notice. Therefore, it behooves the physician to be constantly on the outlook for evidences of pulmonary involvement in the course of these diseases. Exacerbations during any acute infectious disease or in convalescence therefrom should also direct attention to the respiratory organs. In this class of cases, however, it is comparatively easy to detect bronchopneumonia.

From acute simple *bronchitis* it is differentiated by the mildness of the symptoms in the former and by the absence of areas of hyperresonance and dullness in different parts of the chest. In bronchitis the rales are coarser than in bronchopneumonia. It would be futile to endeavor to distinguish between capillary bronchitis, so-called, and bronchopneumonia, for when the bronchioles are inflamed there is always more or less exudate and consolidation, even though the physical signs pointing to these conditions are obscure or wanting.

From *lobar pneumonia*, secondary bronchopneumonia is differentiated by the fact that the former usually attacks persons in good health; that its onset is sudden, severe, and accompanied by a chill; that there is marked prostration in the very beginning of the attack; that the fever is higher and of a continued type, and that it falls by crisis between the fifth and ninth days, most commonly on the seventh; that one lung

only is usually affected; that the sputum has a characteristic rusty color; and that herpes labialis is a very constant lesion.

Great difficulty may be experienced in distinguishing between primary bronchopneumonia with diffuse consolidation and lobar pneumonia. The physical signs in the consolidated areas are identical in the two diseases, but in bronchopneumonia it is common to find signs of localized areas of disease in other portions of the chest. That is the physical signs are diffused or scattered. The character of the sputum constitutes a valuable differential sign, but one which cannot be made use of in children for the reason that secretion is absent or is swallowed instead of being expectorated. It not uncommonly happens that a diagnosis is first made when the temperature falls by crisis between the fifth and ninth day of the illness.

There is a decided similarity between the insidious, subacute forms of bronchopneumonia and tuberculosis. The most valuable means of distinguishing between the two is by examination of the sputum but a bronchopneumonia which persists for more than ten days in a young adult is all too often due to the tubercle bacillus. In suspected cases in which repeated examinations prove negative an injection of tuberculin may be given, provided, of course, that the temperature has been normal for some time. In young children the rarity of pulmonary tuberculosis indicates another type of infection. Small areas of tuberculous consolidation in the apices, together with the associated congestion of contiguous areas, may give rise to subcrepitant rales, and the hectic fever may resemble the intermittent type of that occurring in bronchopneumonia. Careful inquiry into the family and personal history with a thorough physical examination and search for signs of tuberculosis in other parts of the body, will do much to help the physician in making a correct diagnosis.

Small pleural effusions giving rise to crepitant rales, heard at the upper boundary of the effusion when a deep inspiration is taken, may simulate an insidious bronchopneumonia. Exploratory puncture will clear up any doubt which cannot be overcome by other investigations.

Prognosis.—The various factors which determine the clinical course of bronchopneumonia make its prognosis variable, but the disease is always serious. First the *age* of the patient must be considered. At the two extremes of life the mortality is particularly high. In children there is a definite relation between age and mortality; the younger the patients the higher the death-rate. Probably from 30 to 50 per cent. of all cases occurring in childhood terminate fatally. In old age the mortality is exceedingly high. The previous health of the patient and also his surroundings contribute not a little in determining his resistance. All conditions of faulty nutrition, all weakening influences, such as want of fresh air and sunlight, and proper attention to personal hygiene, as well as such constitutional defects as rickets and tuberculosis in other parts of the body, render the prognosis less favorable. Children who are crowded in almshouses, asylums, and charity hospitals do not do so well as when more favorably situated. The immediate cause of the disease also exerts a material influence upon prognosis. The disease is especially

fatal when it occurs in the course of variola, diphtheria, erysipelas and measles, as well as when it ensues as a complication of tuberculosis.

Prognosis is also modified by the extent of the pulmonary inflammation. The symptoms will be more severe and the chances of recovery less when there is massive involvement of the lungs than when there are only a few widely disseminated areas of consolidation. Among the symptoms which augur ill are marked cyanosis, cardiac failure, hyperpyrexia, delirium, convulsions, and stupor. Pulmonary abscess, unless very minute in size, decidedly increases the danger of death, while pulmonary gangrene is always fatal.

Convalescence is slow and relapses are common. In primary bronchopneumonia the mortality is not high and recovery is rapid.

Prophylaxis and Treatment.—Much can be done by adequate prophylaxis to reduce the frequency of this disease. As it is of infectious origin, and as the infection may be endogenous or exogenous, measures directed both to the proper hygienic care of those not diseased and to isolation of the sick will be of use in lowering its occurrence. As concerns individual prophylaxis, the rules of personal hygiene should be strictly observed. Fresh air, sunlight, nutritious food, proper clothing, regular bathing, and sufficient sleep all increase the resistance.

Since microorganisms potent in the production of this disease inhabit the mouth, special attention should be given to buccal hygiene. Careful and regular cleansing of the teeth, with the use of antiseptic mouth-washes, must be insisted upon. The latter are especially important for those predisposed to diseases of the respiratory tract. Disease of the nasal cavities, pharynx, and tonsils must not be neglected, but receive prompt and skilful treatment. Exposure to dampness and cold must be avoided. Persons predisposed to pulmonary disease should keep away from those suffering with pneumonia.

As great a degree of *isolation* as is compatible with existing conditions and hospital facilities should be practised. An ideal method would be to care for a small number of patients in large, well-ventilated pavilions, thereby doing away with the disadvantages of overcrowding and securing adequate isolation. Departments in hospitals for contagious diseases might be reserved for patients who develop pneumonia. No doubt its frequency as a complication of the acute infectious fevers in special hospitals would be diminished if this method could be adopted, as it would remove the risk of contact infection.

In regard to prophylaxis in the aged and infirm the above rules of hygiene also apply. In addition it is important to prevent this class of persons, whenever possible, from maintaining the dorsal decubitus for long periods of time. Much can be done, too, to prevent the super-vention of bronchopneumonia in convalescence from acute diseases. For this purpose warm clothing and avoidance of exposure to cold are of the utmost importance. The use of antiseptic mouth-washes should never be omitted. A child should never be allowed to lie for any length of time in the same position, especially the dorsal, but should be turned at short intervals. No case of bronchitis in a child should be regarded as a trivial affection.

When bronchopneumonia has actually developed the patient should be in a warm, well-ventilated, and well-lighted room, preferably one which is heated by an open fireplace. The hot, dry, and not infrequently dust-laden air of rooms supplied with furnace heat is very irritating to the respiratory tract, makes the patient uncomfortable and increases the severity of his disease. Steam, either natural or medicated, diffused from a bronchitis kettle, keeps the air of the room moist and makes the patient's breathing easier. If medicated steam is desired, a few grains of menthol or a half dram of tincture of benzoin may be added to the water. Exposure to draughts must be avoided and the temperature of the room must be kept equable.

Our therapeutic efforts must be directed to sustaining the patient's strength, to combating toxemia, and to limiting the extent of the pulmonary lesions. For the first purpose nutritious, easily digestible food, with the judicious use of stimulants, is of the highest importance. Milk, koumyss, meat juice, strong broths, and cocoa are suitable articles of diet. Milk holds first rank, but the others may be given alternately with it to prevent the patient from becoming tired of an unvaried dietary. The simple carbohydrates such as rice, barley and oatmeal gruels should be employed as well as proteins. All food should be given in small quantity every two or three hours.

Hydrotherapeutic measures, and heat and cold are among our most valuable resources in combating this disease. Cool sponging will reduce temperature, lessen toxemia, and allay restlessness. Antipyretic drugs should not be used. An alternate hot and cold plunge may be employed, to rouse a child and aid him to expel bronchial secretion. It should be used only in suffocative cases and not repeated often. An ice-bag to the head will diminish cerebral congestion, lower temperature and relieve pain. Saline rectal infusions are valuable for overcoming toxemia, and stimulating the kidneys, not more than 250 cc. of solution should be given to children. If used for infants 50 cc. is quite enough.

Drugs are to be used first of all to maintain the patient's strength and meet symptoms which arise as the disease progresses. In the beginning of the attack it is advisable to administer a dose of calomel to clear out the intestines. From $\frac{1}{2}$ to 1 gr. may be given in divided doses to infants and young children; to older children and adults 2 or 3 gr. is not too much.

The most valuable drugs in the treatment of bronchopneumonia are the stimulants, if the circulation is feeble. In those forms originating from the acute infections alcohol is particularly valuable. In such cases it should be pushed to its physiological limit. Even young children can consume a considerable quantity in twenty-four hours without manifesting any toxic effects. Infants less than a year old can take ten to fifteen drops of brandy or whisky in a little water every hour and older children can take from $\frac{1}{2}$ to 1 dram according to their age. It is always to be recalled that food is the best means of support for an infant and alcohol may do harm by distending the stomach.

Other stimulants of value are Hoffmann's anodyne, aromatic spirit of ammonia, and carbonate of ammonia. When the breathing is labored and cyanosis marked, from 15 drops to a teaspoonful of Hoffmann's

anodyne, according to the age of the patient, will often afford relief and improve the color. Aromatic spirit of ammonia in like dose may be used for the same purpose. Carbonate of ammonia, gr. j to v (0.06 to 0.3 gm.), every two or three hours, acts both as a stimulant and an expectorant; it must be well diluted and preferably mixed with a little elixir of orange or syrup of acacia.

When the lungs and bronchi are rapidly filling with mucus, a dose of atropine will often arrest the secretion and tide the patient over a critical period. From gr. $\frac{1}{1000}$ to $\frac{1}{100}$ (0.0001 to 0.0006 gm.) may be given to a child. A moderate dose of caffeine may be combined with the atropine, if desired for its action as a stimulant. Ether and camphor, given hypodermically, are indicated in severe heart failure and digitalis as a slow but persistent cardiac stimulant may be essential in some cases. Inhalations of oxygen relieve dyspnoea and lessen cyanosis.

Expectorants are serviceable after the stage of free secretion is developed in those old enough to expectorate.

When racking, painful cough is present, narcotics must be resorted to. They may be given separately or in combination with the other remedies employed. For young children paregoric is probably the safest; for those who are older small doses of codeine may be given gr. $\frac{1}{8}$ (0.008 gm.) every three or four hours. No remedy is to be given unless there is a clear necessity for its use, nor should it be continued, as a rule, after it has met a need. Let the patient get well. Drugs may help him, but they cannot cure him. During convalescence tonics, such as iodide of iron, arsenic, and cod-liver oil, are indicated. Residence in a warm, dry, southern climate in winter and in the mountains or at the sea-shore in summer will aid complete restoration to health.

FIBROSIS OF THE LUNGS

Etiology.—Under the names pulmonary fibrosis, cirrhosis, or sclerosis, interstitial pneumonia, chronic interstitial pneumonia, fibroid lung, and fibroid pneumonia, is included a condition of the lung which in general is quite definite, but which in its manifestations is so variable that satisfactory classification is impossible. This is due to the fact that every inflammatory lesion in that organ may result in the formation of new fibrous tissue and a majority of them always so terminate. The affection, then, is essentially secondary in character and any etiological division must be based on diverse causative factors. Any classification adopted therefore answers rather to convenience than to scientific accuracy. Certain types of pulmonary fibrosis are predominantly local in origin and development, while others are more diffuse in character.

The *localized* form develops around or in the lesions of focal diseases of the lung, as gummas, abscesses, infarcts, tumors, and parasitic cysts. Small collections of pigment may result in sclerosed patches in the apices, but commonly this material produces a diffuse fibrosis. The apex is the common site of local fibroid tuberculosis, a large majority of adults coming to postmortem possessing small foci of this character in one or both

lungs. Other chronic infections, as actinomycosis, glanders, and leprosy, may induce localized pulmonary fibrosis.

Diffuse chronic interstitial fibrosis is the result of several pathological processes. Lobar pneumonia occasionally terminates in this manner. For some reason, possibly the non-production of autolysins, resolution does not occur and the fibrinous exudate collected in the vesicles during the stage of red hepatization is replaced by fibrous tissue. The connective tissue formation necessarily begins in the alveolar walls, as from this source must be derived the new vessels which appear in the intravesicular new formation. It is held by some that the new tissue is actually formed from the leukocytes in the vesicles rather than from the cells derived from proliferation of connective tissue elements in the walls themselves. Proliferative changes in the alveolar epithelium may for a time be active during this transformation of the exudate, but eventually the new tissue within the vesicles merges with the thickened, enclosing walls, which take a relatively inactive part in the process, and the area becomes entirely fibroid. Usually this lesion is patchy in distribution, but the parenchyma of an entire lobe may be thus obliterated. This condition is termed organizing or organized lobar pneumonia, gray induration of unresolved pneumonia, or simply chronic pneumonia. The last is preferred by some observers who regard the process as practically distinct from the very beginning, in other words, a primary chronic pneumonia rather than an atypical form of the lobar variety. It is by these clinicians said to be more common in debilitated persons; predisposing causes are extreme and long-maintained reduction in temperature and preceding hyperplastic changes in the pleura. Marchand suggests the name chronic fibrous pneumonia.

Chronic interstitial pneumonia due to the inhalation of dust, whether from coal, iron, stone, or other sources, is a relatively common affection considered under the heading of Pneumokoniosis. The fibrosis is due directly to the chronic irritation of the foreign particles in the tissues, the degree depending upon the amount and character of the inhaled material. Somewhat analogous is the connective tissue production in chronic congestion of the lung, which is induced by the coexisting venous stasis and the blood pigment deposited in the tissues; this has been discussed as brown induration. Another cause of pulmonary fibrosis is pressure exerted upon the lung by neighboring structures, as new-growths and diverticula of the œsophagus, tumors of the mediastinum, and aneurism of the large thoracic vessels. Pulmonary fibrosis due to syphilis is found in the lungs of the newborn as the so-called white hepatization, due to thickening of the alveolar walls, or in the adult as a diffuse process, beginning usually at the root of the lung and extending outward toward the pleura. At times this syphilitic fibrosis appears to extend from the pleura inward. In either case it represents better than any other of the types mentioned a primary, uncomplicated fibrosis of the lung. Bronchopneumonia may terminate in fibroid changes in some of the involved lobules. In these cases the fibrosis begins as a chronic bronchitis or peribronchitis, invading later the surrounding parenchyma.

A second type of diffuse sclerosis is that known as *pleurogenous inter-*

stitial pneumonia. As the name implies, the process follows inflammation of the pleura, generally the plastic type. From the thickened pleura the connective tissue increase extends into the lung, affecting first the interlobular septa and second the finer fibrous structure of the organ. This process is by some not regarded as a distinct type of fibroid pneumonia, but in origin it differs materially from certain cases in which the lesion in the lung is very similar, that is, the fibrosis which develops in a lung that has long been compressed by pleural exudate and thereby largely rendered functionless. Here the pleura is also thickened, but there are no adhesions and the pulmonary fibrosis is secondary to the collapse and is general throughout the organ. In the pleurogenous variety the greatly thickened pleura is nearly always firmly adherent to the chest wall and the fibroid areas in the lung can be traced directly inward from the pleura.

Morbid Anatomy.—This varies as does the etiology. In the disseminated forms, which may be bilateral, the affected lung in part or as a whole is more firm than the normal organ and cuts with increased resistance. The fibroid areas, which may be seen through the pleura, appear on the cut surface as grayish masses, distinctly circumscribed or radiating from the bronchi as more or less prominent bands marking the interlobar or interlobular septa. These areas are more frequent in the lower lobes and are commonly pigmented. If they are multiple and extensive the intervening lung is emphysematous. The bronchi not infrequently show moderate dilatation. The organ on removal or incision may show little or no tendency to collapse.

The massive type of pulmonary fibrosis differs from the preceding chiefly in degree. It is necessarily unilateral, and while it may affect only a lobe it usually involves an entire lung. The chest wall over the affected organ is less prominent than normal; it may be distinctly sunken, with resulting depression of the shoulder of that side. The heart, which is commonly hypertrophied, and the attached tissues are drawn far to the diseased side, their usual site being occupied by the opposite lung, which is emphysematous, often to an extreme degree. The pleura over the fibroid lung may or may not be conspicuously thickened. In pleurogenous fibrosis it is very thick and united to the chest wall by adhesions so dense as to be cut with difficulty. When universal pleural adhesions are absent the lung itself may be extremely small, not larger than a fist, and is drawn inward and backward close to the spinal column. It is firm, cuts with great difficulty, and may be airless. The bronchi are usually dilated, at times to such a marked degree that the broniectatic cavities are the most conspicuous features. Evidence of infection is not uncommonly present; this may be pyogenic or tuberculous, more often the latter, and is occasionally manifested by cavity formation. Tuberculosis is often microscopically demonstrable when there is no gross evidence of the disease. In such cases the opposite lung also is usually tuberculous. In the residual parenchyma of the fibrosed lung there is constantly evidence of acute or chronic catarrhal inflammation.

Symptoms. The changes in the lung may be well advanced before any symptoms other than those of chronic bronchitis, with slight short-

ness of breath upon exertion, manifest themselves. The patient may have had a cough of varying intensity for years, being better in summer and worse in winter, but his health has never been seriously impaired. As the sclerosis becomes more extensive and the circulatory area of the lung is progressively diminished the resulting interference with aëration of the blood will give rise to more constant dyspnœa than was formerly experienced; the destruction of elastic tissue likewise contributes to the production of dyspnœa.

As a result of these changes in the lung an abnormal amount of work is thrown upon the right side of the heart, which hypertrophies in an attempt to sustain the burden placed upon it. In course of time compensation may fail, and symptoms of loss of compensation will then be superimposed upon those produced by the pulmonary lesions. As the heart fails gradually, instead of rapidly the access of cardiac symptoms will be slow. The cough and dyspnœa become worse, the patient loses strength and becomes emaciated, may show signs of cyanosis, and in the advanced stages of his malady may become dropsical.

Cough varies with the stage of the disease and the nature of the pulmonary lesions. As already stated it is an early symptom, varies with the season, and becomes progressively worse as the disease advances. If the bronchi are dilated, a condition not at all uncommon, especially when the disease develops as a sequel to bronchopneumonia, the cough assumes a paroxysmal type owing to the effort necessary to force the secretion from the cavities in which it has collected. Under these circumstances it is often worse in the morning than at other times. Retained secretions may undergo decomposition and give rise to fever, which, however, is not of intense degree, the temperature rarely rising higher than 102°. Fever, if present, is due to the presence of various pathogenic organisms.

In the early stages there is nothing characteristic about the *sputum*, unless perchance the primary cause is some form of pneumokoniosis, in which case it will be stained by one of the pigments present in this latter affection. When there is bronchiectasis the sputum is especially profuse and of a mucopurulent character. If the sputum be retained long in a cavity or if the walls of the cavity ulcerate it may become very offensive, and may be blood-stained if minute vessels are eroded. Blood may also be present after failure of the right side of the heart.

Physical Signs.—When fibrosis of the lung is at all extensive it is accompanied by marked changes in the configuration of the thorax. The contraction and retraction of the lung produce a space in the cavity of the chest, between the surface of the lung and the internal aspect of the thoracic wall, as a result of which the wall retracts. This retraction is particularly marked when there are extensive pleural adhesions. As a rule, the greatest degree of retraction is observed anteriorly between the clavicle and the sixth rib, and posteriorly below the angle of the scapula. The shoulder droops; the intercostal spaces are narrowed; the lateral thoracic wall loses its normal arch, being angular instead of rounded; the apex of the sternum is pulled to one side, and the spine deviates laterally. The respiratory movements are diminished on the

affected side. The position of the heart is also altered. When the left lung is affected the apex beat will be displaced upward and outward. Owing to the retraction of the anterior border of the lung the pulsation of the pulmonary artery may be seen in the second intercostal space. When the right lung is affected the heart will be pulled downward and to the right; displacement may be so marked that the condition may strongly resemble congenital dextrocardia.

Palpation often shows that tactile fremitus is increased. Upon percussion various notes will be elicited. Over the areas of fibrosis, normal resonance is diminished, or perhaps dulness may be present, especially if the area is large and superficially situated or when the pleura is greatly thickened. Areas of compensatory emphysema give a hyperresonance or sonorous sound, while bronchiectatic cavities may emit an amphoric note. When the process affects the right lung the liver ascends and the area of hepatic dulness is higher than normal and perhaps may be continuous with pulmonary dulness. When the left lung is contracted, the stomach and intestines ascend, with the result that tympany is heard over the lower portion of the thorax, dulness or impaired resonance being confined to the superior portion of the chest but this area may be hyper-sonant if the lung is retracted from the chest wall.

The results of auscultation are not distinctive. The vesicular murmur is diminished and bronchial breathing may be detected if there is an extensive area of fibroid lung. Over a bronchiectatic cavity amphoric breathing may be heard. Rales and rhonchi of various kinds will be present during the different stages of the disease, as well as when exacerbations occur.

These in general are the physical signs met with in the different forms and various stages of the disease. Their presence depends in part upon the cause of the pulmonary lesion. Thus, dilatation of the bronchi and its accompanying signs are more common when fibrosis develops after bronchopneumonia, deformity of the thorax more pronounced when it occurs as the result of pleurisy with adhesions, and the area of impaired resonance more sharply limited when it follows an unresolved lobar pneumonia.

Complications.—Softening of the indurated areas may occur, or tuberculosis be superimposed upon the sclerotic (or softened) areas. Bronchiectasis and cardiac changes have already been considered.

Diagnosis.—In well-developed cases of cirrhosis of the lung in which an accurate history of the development of the disease is obtainable, diagnosis may be made at once with reasonable certainty. In other cases it may be very difficult. The diseases from which it must be distinguished are chronic pleurisy with retraction of the lung, new-growths, syphilis, and tuberculosis.

In chronic *pleurisy* with retraction the lower portions of the lung are the parts most likely to be affected, whereas in cirrhosis the upper areas are commonly the site of the disease. Moreover, in chronic pleurisy bronchial breathing is not heard, and the breath sounds may be weak or even inaudible. Hemoptysis, although not uncommon in cirrhosis with bronchiectasis, does not occur in pleurisy.

Tumors of the lung and costal pleura often produce contraction and retraction of the lung. Owing to the pressure which they exert and also to the interference which they cause with the ingress of air into the lung, the alveoli collapse, with the result that symptoms and signs similar to many observed in cirrhosis manifest themselves. Under these circumstances differential diagnosis may at first be very difficult, particularly in the absence of an adequate history. In case the growth is malignant, involvement of the neighboring lymph glands, signs of mediastinal compression, and the cachexia of malignant disease are the greatest helps in making a correct diagnosis. The history of the case, provided that an intelligent and authentic account can be obtained, is also of great value, particularly information relative to the mode of onset and evolution of the disease. *Syphilis* may produce sclerosis of the lung, giving rise to symptoms exactly the same as those found in other forms of the disease, and unless a syphilitic history can be obtained, signs of syphilis found in other parts of the body, or the Wassermann reaction obtained, no definite knowledge can be had in regard to the origin of the pulmonary disorder.

In all these patients resort should be had to an roentgen-ray examination, not only using plates but, more important, the fluoroscope.

The discrimination between beginning sclerosis and *incipient tuberculosis* may present many difficulties. Given a patient who has had an attack of croupous pneumonia from which he has never fully recovered, with more or less persistent cough, some difficulty of respiration as time elapses, perhaps slight elevations of temperature, and presenting such physical signs as areas of consolidation, exaggeration of vocal fremitus, and alteration of normal breath sounds, the question which arises is whether he has pulmonary tuberculosis or is beginning to feel the effects of a sclerotic process in the lung. Unless the tubercle bacillus can be found in the sputum, time alone can decide this question. Tuberculosis may be superimposed upon cirrhosis of the lung, and in cases of long standing in which bronchiectatic cavities exist and fever is present, its association may not be suspected unless examination of the sputum reveals the tubercle bacillus. In fibroid tuberculosis the deformity characteristic of advanced sclerosis is absent, although in the former disease there is often some flattening of the infraclavicular spaces. The symptoms and signs of the two affections are very similar, and in the earlier stages one may easily be confounded with the other.

Prognosis.—Cirrhosis of the lung is incurable, but its progress may be so slow as not to interfere materially with health for many years. This is especially true of the pleurogenous form.

When the disease develops after pneumonia, either lobar or lobular, its course is not so protracted as when it follows pleurisy. Tuberculosis is frequently superimposed upon lobar sclerosis within a short time of the onset and dilatation of the bronchi is often associated with the lobular form. Both these conditions contribute to the severity of the disease and tend to shorten the duration of life. Cardiac complications may cause death in the more advanced cases.

Treatment.—It having been stated that cirrhosis of the lung is an incurable malady attempts to limit its development should be made. As the disease is known to develop after incompletely resolved pneumonia, no pains should be spared to secure resolution in every case. Respiratory gymnastics, residence in a warm, equable climate, with the administration of such drugs as cod-liver oil, arsenic, syrup of hydriodic acid, or iodide of iron are appropriate measures.

Hygienic measures are of the utmost importance. If the patient's means permit, he should permanently reside in a warm climate where variations of temperature do not prevail, and where there is not much alteration in the humidity. If secretion be profuse, a dry climate, like that of Arizona, for instance, is suitable. High altitudes are contraindicated for persons in the advanced stages of the disease because of the decrease in lung area and the cardiac complications. It is important that the air shall be pure and free from dust. Those who cannot change their residence should at least endeavor to obtain as much fresh air and sunshine as they can, and to relinquish occupations entailing the inhalation of dust-laden air. They should remain indoors in inclement weather and should be warmly clad. It is important to maintain bodily nutrition at the highest possible level, and to secure this end a generous diet should be provided. Highly seasoned, rich, and indigestible food must not be eaten. Tobacco in excess must be interdicted but alcohol in some agreeable form aids digestion.

The tonic hydrotherapeutic measures, such as the half-bath of moderate temperature with sprinkling of the breast and back with cool water, and later, as the patient becomes more accustomed to the treatment, the use of cool or cold affusions are of decided value in improving nutrition and lessening the liability to contract cold.

As regards treatment by *drugs*, the early stages of the disease are best managed by the employment of stimulating expectorants for the bronchitis, such as benzoate of ammonium, in 10-gr. doses (0.6 gm.) given in capsules after meals, or 5 minims of oil of sandal (0.3 cc.) administered in the same manner. If secretion is profuse, terpin hydrate may be employed instead. Small doses of codeine may be necessary to alleviate the cough. For acute exacerbations of the bronchitis, ipecacuanha or carbonate of ammonium will be found useful. Inhalations of turpentine or carbolic acid may be employed when bronchiectatic cavities are present. Digitalis must be used according to the usual rules when cardiac compensation begins to fail.

EMPHYSEMA

In the consideration of pulmonary emphysema at least five types, so-called, of the affection are to be noted, namely: (1) Hypertrophic substantive, idiopathic, or large-lunged emphysema; (2) senile or small-lunged emphysema or senile atrophy of the lungs; (3) compensatory or vicarious emphysema; (4) acute vesicular emphysema; (5) interstitial or interlobular emphysema. Although all but the last named of these affect the vesicles, the first only is a distinct pathological and clinical

entity for which the term emphysema is entirely appropriate. This type is very clearly differentiated from the others and to it reference is always made when the unqualified term emphysema is employed. For these reasons it seems wise first to consider this form and later briefly to state the chief characters of the other varieties.

1. **Substantive or Large-lunged Emphysema.**—**Etiology.**—Very many factors have been assigned as the chief or contributing cause of this disease. Two points appear definitely established, namely, that emphysema occurs rarely or never in lungs that are not congenitally weak, and, second, that the actual exciting cause is increased intravesicular tension. So far as the first factor is concerned the disease is hereditary in that the predisposition is transmitted in the shape of pulmonary tissue that is unable successfully to withstand heightened intra-alveolar pressure. This view receives strong support from the number of family series of cases reported and also from the not infrequent development of the disease in childhood. The condition in the parents most often underlying this tendency is emphysema itself, but gout appears worthy of mention. The fundamental nature of the inherited weakness has not been clearly determined. A defect in the elastica of the lung is the most reasonable supposition, and although this has not been proved and possibly is incapable of satisfactory demonstration, it nevertheless best explains the changes that occur. Heightened intravesicular pressure may be brought about by forced inspiratory or expiratory action. This is undoubtedly active in the production of compensatory emphysema, but that it is of considerable importance in this type is to be regarded as doubtful. When lobules or parts of lobules are eliminated from the air-containing capacity of the lung by varied processes, particularly in the nature of inflammation of the smaller bronchioles, the neighboring vesicles become at least temporarily overdistended. This is admitted by all, and if the plugged areas remain permanent, typical compensatory emphysema results elsewhere. To induce a universal distribution of the lesion, the obstruction must shift, and thus in succession bring all parts of the lung under the increased strain. If this repeatedly occurs the elasticity of the vesicular walls finally become permanently lessened and an overdistended condition of the vesicles is the result. From the very nature of this process it does not appear that it can be held accountable for the production of the great majority of the cases of large-lunged emphysema.

The *expiratory factor* in the production of increased intravesicular tension and consequently of emphysema must be regarded as a more satisfactory explanation. It is brought about by increased pressure upon the lung by the chest wall at the time when free egress of air from the organ is prevented by abnormal conditions in the respiratory passages, particularly the narrowing of the glottis that occurs during coughing. By inducing the violent expulsive efforts made during this act, chronic bronchitis is one of the most fruitful causes of emphysema. Asthma is a very frequent cause, as is also whooping cough. Long continued asthmatic attacks induce a chronic emphysema, whereas that induced in young children by whooping cough is often of moderate degree and temporary. During these efforts the sternum and costal cartilages are pushed

forward, the ribs become less oblique, the outer and posterior parts of the lungs are subjected to increased pressure, and the spaces in which lie the apices and anterior margins of the organs are made more capacious, thus permitting overdistention of the vesicles in those areas. Confirmative of this explanation is the fact that in these locations emphysema first appears and later becomes most conspicuous. The increased tension produced in the lungs of glass-blowers and the players of wind instruments, as well as that induced by heavy lifting also tends to produce emphysema. That they are not so important as at one time believed, however, is borne out by recent clinical and anatomical studies, it being shown that with care a wind instrument can be blown without injuring the lungs of the player. It may be said that doubtless in some cases both inspiratory and expiratory distention are active in the production of emphysema, the former especially in those parts of the lung subjected to greatest pressure by the thoracic wall. In chronic bronchitis there is not infrequently the foundation for both series of phenomena.

In the etiology must be included those conditions which tend to produce bronchial or other changes that in turn cause increased expiratory effort. Among these should be mentioned the inhalation of the various forms of dust. Regarding age, substantive emphysema more frequently develops in early and middle adult life. That in old persons is commonly of the type of senile atrophy of the lung. Rapidly developed emphysema, as would be inferred from what has been said regarding hereditary weakness of the lung, is more apt to occur in children, but, as pointed out by Hoffmann, these subjects in many instances make a partial or complete recovery instead of passing on into the chronic form of the affection. As to sex it is probable that women are less often affected only because they are less exposed to exciting causes.

Morbid Anatomy.—The emphysematous lung is excessively large and does not collapse when the chest wall is opened. The anterior margins of the two organs may meet or even overlap, these portions, together with the apices and to a lesser extent the basal margins, being particularly affected. The increased space they occupy is obtained by the displacement forward of the sternum, the more horizontal position of the ribs, and the crowding of the heart to the unaffected side if the lesion be unilateral or downward if bilateral; the diaphragm is also depressed. The costal cartilages are often calcified. The pleura over the emphysematous areas is dry and pale and often contains no pigment; when the pigment is absent the condition is known, after Virchow, as pulmonary albinism. The affected areas, although not commonly cedematous, pit on pressure, a proof of the loss of elasticity. Congestion is not usually present, and, unless it is, the lung is decidedly paler than normal. The organ is below the average weight and to the palpating finger has a peculiar spongy feel well described by Laennec as that of a pillow of down. Crepitation is lacking in the most emphysematous areas, the contained air readily passing from place to place under advancing pressure. Along the margins may be found prominent bullæ varying in diameter from 0.5 to 2 cm. These are formed by the coalescence of distended vesicles and in contradistinction to the somewhat similar appearing blebs in interstitial

emphysema cannot be made to change their location. When the organ is incised many of these bullæ do not collapse, but remain as distinctly outlined spaces. The increased size of the individual vesicles exposed on the incised surfaces is apparent to the naked eye. The smaller bronchi may also show dilatation.

Histology.—Microscopically two lesions are conspicuous. The first is atrophy of the vesicular septa which show varied degrees of thinning. Many of them largely disappear, leaving only short ends projecting into the space formed by the coalescence of the alveoli which originally were divided by the septum. In this way the union of a large number of vesicles produce the bullæ previously mentioned. The loss in septal tissue means also a diminution of the vascular field of the lung and consequent imperfect aëration of the blood, this is part explaining the accompanying dyspnœa. The second lesion of importance consists of changes in the elastic tissue. The fibres of this substance lose their normal, wavy outline, become swollen, and often undergo fragmentation. In marked degrees of the change, elastica as such entirely disappears, only a few granular fragments marking the site of the former fibrils. This is a second factor in the production of dyspnœa, the weakened lung being unable properly to contract and thus increasing the amount of residual air, the tidal air being correspondingly diminished. The bronchi are commonly inflamed and usually show thickening of the walls; the smaller tubes may be dilated. Pigmentary infiltration is commonly slight.

Associated Lesions.—These are hypertrophy with dilatation of the right heart or possibly of the entire organ; atheromatous changes in the pulmonary artery with, in some instances, dilatation of that vessel; changes including pigmentation, atrophy, and fibrosis in the liver, spleen, and kidney depending upon congestion secondary to the obstructive lesion in the lung.

2. Senile or Small-lunged Emphysema.—This is a disease affecting old persons, and, although it possesses some of the histological features of emphysema, would more correctly be grouped as senile atrophy of the lung. The chest presents a condition entirely different from that in the type just described. It is small, the ribs are more oblique than usual, and the attached muscles are wasted. The lung is decidedly smaller than the normal organ; it collapses when exposed and not infrequently contains accompanying lesions, as congestion, œdema, or even infarction. The intervesicular septa are atrophied and broken and the resulting coalescence of numbers of alveoli gives rise to large spaces with remnants of vesicular walls showing on the inner surface. These large bullæ may be so numerous and extensive as to almost entirely constitute the lung. The bronchi are often dilated. The septal atrophy here appears primary, the resulting large spaces being thus produced without the intervention of heightened air pressure.

3. Compensatory Emphysema.—This is the form that develops in portions of the lung when other parts are airless and is quite satisfactorily accounted for by the inspiratory theory. It may be temporary in point of duration, as when developing in the unaffected lobules in cases of bronchopneumonia. In such instances it is really a physiological over-

distention with stretching of the alveolar walls, which on withdrawal of the cause assume their normal condition. More often, however, it is lasting, the vesicular walls undergoing atrophic changes. The latter type is seen in the lung in cases of new growth, especially of multiple metastatic nodules, between and around tuberculous areas or isolated fibroid patches, and particularly in chronic fibrosis. In the presence of pleural adhesions the condition also develops.

4. **Acute Vesicular Emphysema.**—This condition clearly should not be placed in the group where long-continued usage still keeps it. It is a functional overdistention of the air vesicles coming on rapidly in cases of acute bronchitis or asphyxia or at times during attacks of angina pectoris or of asthma. Relief or death ensues before the vesicular walls atrophy and consequently the affection is not truly emphysema.

5. **Interstitial Emphysema.**—This is characterized by the presence of air in the connective tissue of the lung and is due usually to the rupture of air vesicles during violent expiratory efforts in coughing. The distended vesicles in vesicular emphysema may give way and thus allow the air to reach the abnormal location. The condition is also caused by wounds of the lung from without, as by fractured ribs or other penetrating objects. As pneumothorax may arise from pleural infection by gas-producing bacteria it is possible that their presence in the connective tissue of the lung might cause an interstitial emphysema. This type of emphysema is readily diagnosed postmortem by the presence beneath the pleura of variously sized blebs, sometimes 2 cm. or more in diameter, which by pressure can be made to change their place, thus differing from the stationary bullæ in vesicular emphysema. Rupture of these blebs may produce spontaneous pneumothorax, and when near the root of the lung, air occasionally passes into the mediastinum and even the structures of the neck, giving rise to emphysema of those tissues.

Symptoms.—As the evolution of the disease is slow, its symptoms do not manifest themselves abruptly but are of gradual onset and progressive development. It is not unusual for patients to suffer ill health a long time before distinct evidence of emphysema can be elicited.

One of the chief symptoms is *dyspnœa*. In the beginning of the disease, before pulmonary distention has become far advanced, it may amount to no more than slight shortness of breath upon exertion, but as the lungs lose more and more of their elasticity and the capillaries in the alveoli become obliterated, it grows constantly worse. In a person suffering from advanced emphysema, inspiration is short and quick, while expiration is much prolonged. This peculiarity in breathing is due to loss of elasticity in the lung, upon which expiration largely depends. When this attribute is lost the air is not expelled from the lungs in a normal manner, all the auxiliary forces of expiration being summoned into play. Even then the result is not complete and a certain excess of residual air remains. When the dyspnœa becomes unusually severe, especially during a paroxysm of asthma or with an exacerbation of bronchitis, the patient will often be found pressing forcibly upon his sides in an endeavor to drive more air out of his lungs. The most characteristic circumstance about the dyspnœa therefore is that it occurs with expiration.

A considerable influence is exerted upon the intensity of the dyspnoea by the degree of severity of the associated bronchitis; thus when exacerbations of the latter occur and the secretion becomes more copious, the difficulty of respiration will be augmented, whereas, on the other hand, during periods of comparative freedom from cough and bronchial catarrh only slight dyspnoea is experienced. There is nothing peculiar about the cough. As it is more or less constant, it not only harasses the patient, but saps his strength as well, and hastens the development of cardiac complications. The sputum is that of ordinary chronic bronchial catarrh except in those cases in which asthma is present, when it may contain Charcot-Leyden crystals and Curschmann's spirals.

The heart suffers as well as the lungs, and symptoms of circulatory disturbance are characteristic of the later stages of the disease. The weakness of respiration, the mechanical effect of the retained air upon the lungs, the paroxysms of coughing, all serve to make aëration of the lungs defective and consequently diminish oxygenation of the blood. This is at first shown by blueness of the lips and slight lividity. Upon severe exertion the lividity may become so augmented as to constitute distinct cyanosis, and it is likewise increased when exacerbations of the bronchitis occur.

As more and more bloodvessels in the lungs become obliterated, and as an increasing number of alveoli become distended, the work of the right side of the heart is progressively increased. It undergoes hypertrophy to overcome the resistance with which it has to contend, but sooner or later compensation fails because the destructive process in the lungs is unlimited in its potentiality of development, whereas the heart can only hypertrophy to a certain extent; moreover, the functional disturbances engendered by the pulmonary lesions are so violent as to vanquish the saving effort put forth by the increased cardiac action. Thus it is that compensation fails and the heart dilates. Under these circumstances the dyspnoea and cough becomes more distressing and the cyanosis more pronounced. Digestive and intestinal disturbances ensue. The liver becomes congested, the extremities swell, and dropsy sometimes occurs. Nutrition suffers and the patient grows weak and emaciated. Hemoptysis and hematemesis sometimes take place; epistaxis, too, is not uncommon when there is much venous congestion. Hemorrhoids also are frequently associated with emphysema, being due to hepatic congestion.

Physical Signs. The thorax presents marked abnormalities, the anteroposterior diameter being much increased, so that it may equal or even exceed the lateral diameter. It is only in exceptional cases, however, that a tracing with the cyrtometer shows equality of the two diameters. The shoulders are rounded, the curve of the spine increased, the clavicles prominent, and the subclavicular spaces obliterated, and the supraclavicular spaces often depressed; the sternum and ribs bulge out anteriorly and the intercostal spaces are widened. These changes give the chest a barrel shape, and make the neck look unusually short. Owing to cardiac disturbance the superficial veins become dilated and stand out prominently on the skin. They show very plainly in the neck,

distention sometimes occurring with each expiration, so that they have the appearance of pulsating tumors. Pulsation in the epigastrium is also frequently noticed. Instead of expanding with the act of inspiration the chest becomes elevated and its lower part may even retract when an inspiration is taken.

Palpation will sometimes show that vocal fremitus is diminished, although it frequently happens that no abnormality in this respect is demonstrable.

The percussion note is increased in resonance, or may even be distinctly tympanitic. The pulmonary area is always increased, often extending posteriorly to the lower costal margin and reaching anteriorly to the level of the sixth or perhaps the seventh rib. The area of cardiac dullness is greatly diminished and may be entirely obliterated. Even when the heart is enormously hypertrophied it may happen that only a small area of cardiac dullness can be detected owing to the fact that the distended lungs almost entirely cover it.

The diaphragm is at a lower level than in health and the liver dullness often begins in the seventh costal interspace. The area of splenic dullness cannot, as a rule, be well defined owing to the distention of the lung on the corresponding side. The stomach is often dilated, but it cannot always be outlined for the same reason that it is not always possible to make out the boundaries of the spleen.

Upon auscultation the breath sounds are found to be weak. The inspiratory sound is short and labored, the expiratory sound prolonged and feeble. As bronchitis is frequent, rales are often heard in all parts of the chest. A peculiar crepitant sound which has been attributed to friction of the distended portion of the lungs upon the pleura is also sometimes present. The cardiac sounds are feeble owing to the distended lungs covering more or less of the heart. As cardiac involvement becomes more pronounced, the signs of tricuspid insufficiency appear.

Complications.—The distinct complications are pneumothorax and interstitial emphysema. The former results from the rupture of pulmonary vesicles, the latter sometimes follows a violent paroxysm of cough or overexertion.

Diagnosis.—The general appearance of a person suffering with advanced emphysema with the symptoms and the signs usually suffice to prevent the disease from being confounded with other affections. The characteristic dyspnoea, the cyanosis, and the shape of the thorax make a picture which is not formed by any other disease. There is, however, a disease which presents some symptoms and signs common to emphysema, namely, pneumothorax, but its onset is usually sudden instead of gradual, it is limited to one side of the thorax, and the deformity which stamps emphysema is not present. Further, in emphysema the intercostal spaces are not obliterated as they are in pneumothorax.

Fränkel states that extensive adhesions of the parietal pleura to the lungs may give rise to symptoms closely resembling those of emphysema and cause hypertrophy and dilatation of the right side of the heart. When the entire surface of the pleura is not adherent, the relatively free portions of the lung may become distended. If it happens that only

the lower portions are adherent, the upper part of the lungs may become distended and produce alterations in the conformation of the upper part of the thorax. This condition, however, must be exceedingly rare. It would be differentiated from emphysema by the absence of the physical signs relating to the lower part of the pulmonary area. If of long duration, however, the process would amount to the same thing as a moderate degree of emphysema. The symptoms produced by the pressure of tumors upon the trachea and larger bronchi ought not to be mistaken for emphysema, for although dyspnoea is present and the vesicular murmur diminished there is no general deformity of the thorax.

Prognosis.—Emphysema is incurable, but much can be done to render the patient comfortable and to prolong his life. Even when left to pursue its course unhampered it is not a rapidly fatal disease; so that persons affected with it often live for years, although their existence is always shortened. Seasonal changes exert a material influence upon the comfort of emphysematous patients and likewise upon the severity of their disease. In winter the bronchitis is more subject to exacerbations than it is in summer, and for this reason patients are often worse during cold weather. As long as cardiac compensation is maintained there is no immediate danger of death unless some complication sets in, such as bronchopneumonia or influenza. Dropsy and pulmonary hemorrhage are very serious complications.

Treatment.—As emphysema is an incurable malady the efforts of the physician should be particularly directed to preventing its development in those who are predisposed by reason of chronic bronchitis and asthma, and also to delaying, as far as it is in his power, the evolution of the disease when it is detected in its incipient stage. A careful regimen will greatly reduce the liability of the development of emphysema and also materially prolong the days of those who are subject to it.

Persons affected with chronic bronchitis or asthma should take the utmost pains to avoid exposure to cold and dampness, and should be constantly on their guard against sudden changes of temperature. Those whose means permit it should spend the colder months of the year in a warm, sheltered climate at a moderate elevation, such as that of Egypt and the Riviera, or Southern California. If the cough is very dry and expectoration scanty, moist climates are suitable. In summer, residence in localities situated near pine forests is desirable. The altitude must be moderate and not high, and a place should be selected where strong winds do not prevail. The Maine woods and the Adirondack mountains are suitable places for summer residence. During bad weather these persons should not venture out of doors. They should be warmly clad at all times. Occupations demanding great physical exertion and those in which there is exposure to dust or irritating fumes should be relinquished.

The diet should be substantial, but composed of food that is easily digested. The bowels must be regulated, laxatives being used if necessary. These rules also apply to those who already have the disease.

Different mechanical appliances have been employed to facilitate the expulsion of air from the lungs. Thus an elastic belt has been worn

around the lower part of the thorax, and Strümpell's apparatus, consisting of two boards joined at one end by an elastic band, had been used, one board being placed on each side of the thorax and pressure made during expiration by the patient grasping the anterior ends and bringing them forcibly against the body. A more elaborate apparatus devised by Steinhoff has been used also for the same purpose. The effort made often increases the dyspnoea. Swedish movements, consisting of direct pressure upon the ribs or forcible rotation of the trunk upon its axis alternately from one side to the other, have been employed for the purpose of immobilizing the ribs, and thus arresting the changes in the configuration of the thorax. Such methods are futile.

Hydrotherapeutic measures are valuable as they exert a favorable effect upon the heart and circulation. Hot and cold douches, the cold rub, and the cold half-pack have all been used with benefit. They should not be employed as a routine, but should be selected for individual cases as the physician may deem advisable. The hot douche has been used with good results with some of the pneumotherapeutic measures.

Various methods of pneumotherapy have been used, and it has been asserted that brilliant results have followed their employment. The condensed-air bath was highly recommended by Dujardin-Beaumetz, but it is doubtful if any good results follow its use other than those which depend upon its stimulating effects upon the bronchi. The distention of the lungs cannot be influenced by it. For the subjects of advanced cardiac disease and arteriosclerosis it is dangerous.

Expiration into rarefied air has been tried, both alone and in conjunction with the condensed-air bath. It causes retraction of the thorax, and increases the force of expiration, thus causing more air to be expelled. This method seems rational and, indeed, some of its strongest partisans have asserted that most brilliant results have been secured by its employment. That many of the assertions as to its value were extravagant has been proved by further experience and investigation. Temporary relief is afforded in some cases by the inspiration of rarefied air, but in others no benefit is derived. All these measures require apparatus which practitioners never have.

The inhalation of mineral waters by atomization and vaporization also requires mention. Sulphur and arsenical waters have been extensively used in France for this purpose, and it is stated that relief has often followed their employment. They are inhaled in the form of a fine spray, and are also vaporized. It is not to be doubted that they frequently relieve the symptoms of bronchitis. At Luchon, in France, the inhalation of sulphuretted vapors by the method known as "humage" has been practised, and is said to afford good results. It is not improbable that the regimen of living at these resorts, with the baths and internal use of mineral waters, contribute to bring about a large part of the relief.

Venesection is valuable for the relief of severe dyspnoea and cyanosis. The extraction of a pint of blood will sometimes save a patient who is gasping for breath, and so cyanosed that he is black in the face. Venesection should not be used in any but the most severe cases.

The treatment of the disease by drugs must be directed to combating symptoms as they arise. As a matter of fact the therapy of emphysema is fruitless. The treatment of the bronchitis and cardiac state is often of great value. Bronchitis and asthma must be combated, and circulatory disturbances controlled as much as possible. Exacerbations of the bronchitis are to be treated by the use of expectorants, such as ipecacuanha and small doses of apomorphine, by counterirritants such as turpentine liniment or mustard applied to the chest, and by sedative inhalations such as a mixture composed of equal parts of compound tincture of benzoin and paregoric, of which a tablespoonful is used to the pint of hot water. When there is profuse secretion of mucus in the bronchi, an emetic dose of apomorphine will sometimes cause its expulsion and afford relief. For the associated chronic bronchitis ammonium chloride is probably as good a drug as we possess, it may be given in 5-gr. doses every four hours, and if the cough is very distressing, gr. $\frac{1}{6}$ (0.01 gm.) of codeine sulphate may be added. This drug may be administered in fluid-extract of licorice or syrup of wild cherry. Terpin hydrate and creosote may sometimes be used with advantage. Sandal-wood oil is very useful. The thing to be feared about all these expectorants is that they may disorder the stomach. If they do they must be stopped at once.

For an attack of asthma a hypodermic injection of 5 to 10 minims of epinephrine solution (1 to 1000) or gr. $\frac{1}{4}$ (0.016 gm.) of morphine and gr. $\frac{1}{1000}$ (0.0006 gm.) of atropine maybe administered, and if the condition of the heart does not contraindicate it, a few whiffs of amyl nitrite also may be given. For failing cardiac action, digitalis in small doses and strychnine fulfill all indications; 5 drops of tincture of digitalis three times a day will prolong the patient's comfort for a considerable period. Large doses of strychnine, for instance, gr. $\frac{1}{20}$ (0.003 gm.) three or four times a day, for a short time are often useful. It is not at all uncommon for marked improvement in the bronchitis to take place under the use of these drugs.

When dilatation of the heart has occurred and venous congestion is marked, larger doses of digitalis are indicated and 10 to 15 minims may be given every four hours. Digitalis is often less efficient in the cardiac disease of emphysema than in other forms of heart disease, for the reason that it does not materially influence, and certainly cannot arrest, the lesions in the lungs upon which the heart trouble depends and also because myocardial degeneration has progressed as an associated lesion in many instances.

The iodides have long been employed in the treatment of emphysema. At one time it was thought that they might prevent destruction of the pulmonary vesicles, but such a theory is not tenable. The good which follows their administration depends upon the effect they exert upon the bronchitis and upon their action on the bloodvessels. They lower arterial tension and may retard the development of arteriosclerosis. Five grains (0.3 gm.) of the iodide of sodium or ammonium may be given in water or milk after the meals. The syrup of hydriodic acid may be substituted when the ordinary iodides disagree.

GANGRENE OF THE LUNG

Etiology.—Gangrene of the lung is due to partial or entire necrosis of a portion of the organ and added infection which probably always is mixed in character, although in one reported case the *Trichomonas intestinalis* was the only demonstrable cause. Necrosis alone, without the phenomena of gangrene and infection by certain of the bacteria which are often found in gangrenous tissue, does not ordinarily give rise to this process. Studies indicate that the saprophytic putrefactive bacteria are a necessary adjunct to the already necrotic and usually previously infected tissue, but no special bacterium which in every case acts as the exciting cause has been isolated. As a consequence, gangrene is found in connection with processes that lower the vitality of pulmonary tissue by interfering with the blood supply and which favor, or actually carry with them, infection of the necessary type. Just why gangrene occurs in certain instances and not in others under what appear to be similar circumstances in both is not perfectly clear. Difference in tissue resistance is the most reasonable explanation.

Among the important causes are: (1) Lobar pneumonia. This disease does not often terminate in this manner; Norris and Farley found 136 instances in 27,761 collected cases. It may or may not be preceded by abscess formation. (2) Aspiration pneumonia. In these cases the causative agents are drawn into the finer bronchi where the process begins. (3) Pulmonary embolism. This is most frequently a cause when the emboli are from a septic focus, but the plugging of a large vessel by a non-infected embolus may induce the condition. Any of the causes mentioned in the consideration of pulmonary infarction, especially if the primary focus be infected, may result in gangrene of the lung. (4) Foreign bodies in the bronchi or bronchiectatic cavities may lead to gangrene. In either case intensely infectious material gathers in the affected area and is propagated into the surrounding tissue. Tuberculous cavities may also act in this manner. (5) Trauma. This may exert its effect in the way of simple contusion of the chest wall or by actual perforation of the wall and direct injury and infection of the lung. (6) Infectious and debilitating diseases, as typhoid fever, diabetes mellitus, and long-continued bronchopneumonia. (7) Suppuration in the lung. (8) Pressure upon the pulmonary vessels by aneurism or new-growths in the lung or in adjacent structures. Gangrene is prone to follow rupture into the lung of cancer originating in contiguous tissues.

Morbid Anatomy.—Gangrene of the lung may be diffuse or circumscribed. The former rarely occurs but may terminate an attack of lobar or bronchopneumonia, affecting an entire lobe or even a whole lung. Occlusion of a large branch of the pulmonary artery may also induce this type. It corresponds to the so-called spreading gangrene of the extremities in that the gangrenous area possesses no definite line of separation from the surrounding structure, the grayish or dark necrotic area passing gradually into the inflammatory zone of recognizable pulmonary tissue that surrounds it.

Circumscribed gangrene may be in the form of single or multiple foci, but in either instance the diseased tissue is sharply separated from the surrounding lung. The affected area is at first brown or slightly reddish in color, but soon becomes dark and finally almost black, liberated pigment from disintegrating blood cells being largely responsible for the coloration. A greenish tinge may appear, but this is usually not so prominent as in the gangrene of external parts. Softening and disintegration soon occur and a cavity is produced. Unless of large size the cavity is not always entirely empty, but contains one or several irregular masses of softened and discolored lung tissue which have not entirely liquefied. In the ragged wall or even passing through the cavity may often be found bloodvessels and bronchi which have resisted the necrotic processes. When cavities are formed, the characteristic sputum appears with the fetid odor of pulmonary gangrene; hemorrhage may occur, the vessels in the affected part not usually being firmly thrombosed. Surrounding the inner wall of the cavity is a zone of congested or hyperemic tissue and external to this an œdematous area. Leukocytes appear in the outer zones, and if the gangrenous focus be small and the reparative powers of the living tissue active, connective-tissue formation with healing of the necrotic area may limit the process and lead to recovery of the patient. This unfortunately is not a common occurrence.

Symptoms.—As in pulmonary abscess, so, too, in gangrene, the manner of onset and the symptoms depend somewhat upon the causes which give rise to its development. Thus when it develops in the course of specific infections, the symptoms of the latter may predominate at first, although pulmonary disturbances may even then be present in lesser degree, for the reason that it is not uncommon for the gangrenous process to be preceded by bronchopneumonia, and because some infiltration is invariably produced in the lung before distinct necrosis takes place. When due to lobar pneumonia, its onset is usually marked by a chill and elevation of temperature some days after the crisis has occurred. When cavities in the lung become necrotic the process is usually slow and marked by gradual increase in the severity of the symptoms previously present.

It will be seen, then, that, as a rule, symptoms referable to the respiratory organs, together with some elevation of temperature, loss of appetite, and weakness precede the more characteristic manifestations of gangrene, and that they may continue for days or weeks before the latter become pronounced. Although the onset is not sudden in the sense that the disease attacks persons who were previously in good health the establishment of the gangrenous process is, however, usually announced by a marked exacerbation of the existing symptoms, which is often very abrupt. The temperature rises higher and chills may occur, the cough becomes worse and dyspnœa sometimes ensues. As soon as the necrotic area communicates with a bronchus the sputum undergoes a change. While up to this time it may have possessed the characteristics of pneumonic sputum, contained a little blood, or merely have been such as is expectorated in bronchitis, according to the individual case, it now is found to possess an attribute peculiarly its own. This property is an extremely fetid odor not met with in any other disease, and which has

been variously described as resembling that of fecal matter, dung-water, or putrefying flesh. This odor is transmitted to the patient's breath, and is so intense and penetrating that it is often diffused through the entire room.

With the supervention of this sign the subjective symptoms become accentuated. Fever increases, the temperature rising perhaps as high as 104° or higher; the pulse becomes rapid, soft, and compressible; the cough more distressing, and exhaustion greater; any attempt to move increases the severity of the symptoms. The face is pale and drawn, the tongue dry and cracked, the extremities cold, and the whole body sometimes covered with a cold sweat. Anorexia is complete and vomiting may occur, both being due no doubt to the foulness of the expectoration. Diarrhœa may also be present. It has been observed that the patient is inclined to lie on the affected side, thereby causing gravitation of the secretion and lessening the frequency of expectoration.

In those patients in whom the course of the malady is prolonged all these symptoms are modified except the foul sputum.

The *expectoration* is usually abundant. When the sputum is first coughed up it is of a dirty gray or brownish color. If it be collected in a glass it separates into three layers: In the bottom of the glass there is a thick, opaque stratum, of a yellow or greenish-brown tinge, consisting of pus, fragments of lung tissue, and gray or yellow grumous masses. Above this stratum is a transparent layer of serous fluid, perhaps having a few flocculi floating in it, while superimposed upon this is a thick, opaque, frothy layer, of a dirty yellow color. Microscopic examination of the lowest stratum reveals the presence of leukocytes, red cells, epithelium, and elastic tissue. Traube called attention to the fact that elastic tissue may be absent, and its absence is attributed by Filehne to the action of a bacterial ferment which he discovered, similar to trypsin. The clot-like plugs are found to contain fatty acids.

A special form of pulmonary gangrene which requires mention is that which occurs in diabetes mellitus. Its course is very chronic, lasting perhaps for many months. It usually begins as a pneumonic process with profuse expectoration of blood-stained sputum, which finally becomes malodorous, although it is never so offensive as that in other forms of the disease. Hemorrhages are of frequent occurrence.

Physical Signs.—In the beginning of the disease examination of the thorax fails to reveal distinctive signs. There may be areas in which the percussion note is somewhat impaired, and upon auscultation moist rales and diminution of the breath sounds may be heard. As the morbid process advances and the pneumonic infiltration around it becomes more extensive, dullness may become more pronounced. This is more likely to be the case when the gangrenous area is superficial than when it is deep. As softening of the dead area takes place and the necrosed tissue begins to be expelled, the signs of cavity formation may appear. The rales become larger and more moist and amphoric breathing and pectoriloquy may be heard. Owing to the accumulation of secretion in the tissue around the cavity, subcrepitant rales may be heard in an area

beyond its borders. Bronchial breathing may be present, as in some cases extensive consolidation exists around the cavity.

Complications.—The principal complications are hemorrhage, empyema, and metastatic abscesses. Hemorrhage is prone to occur; it is due to involvement of bloodvessels in the gangrenous process. When the latter is situated superficially it may extend to the pleura and cause a portion of the latter structure to slough away, with the result that pyopneumothorax is produced. The pleura may also become inflamed without being ruptured, and the effusion which is poured out is generally purulent. Metastatic cases owe their origin to septic emboli resulting from disintegration of blood clots which form in the vessels of the lung. They are commonly located in the brain, although they may occur in the liver, spleen, and kidneys. Their presence in the brain gives rise to cortical irritation, to hemiplegia, and to monoplegia.

Diagnosis.—This rests upon the putrid odor of the breath and sputum and the physical characteristics of the latter. The physical signs of cavity alone are of no worth, because they may be produced by other lesions, but taken in conjunction with the diagnostic points just mentioned they are of corroborative value. The previous condition of the patient and the mode of onset and evolution of his present trouble must be taken into account, especially when the process is not acute. The degree of prostration will also serve as an index.

In putrid bronchiectasis the odor of the breath and sputum is not so foul as it is in gangrene, and elastic tissue is never expectorated; the constitutional disturbances also are not so severe. It may be very difficult to distinguish between cases of ulcerating tuberculous cavities and gangrene, although the tubercle bacillus may be found in the sputum of the former disease. Tuberculous cavities may, however, become gangrenous, and in this case the bacterial findings are of little value.

Prognosis.—Gangrene of the lungs is a very fatal malady. In the acute form death usually occurs within a few days after the development of the disease. It may result from hemorrhage, acute toxemia, or complications such as pneumothorax or metastatic abscesses. In the subacute and chronic cases the patient may die from exhaustion or sepsis after weeks of illness. When the lesion is small and circumscribed recovery may take place.

Treatment.—Little can be expected from medical treatment. The patient's strength should be maintained, if possible, by the use of highly concentrated liquid food, given in small quantities at frequent intervals, with the liberal administration of alcohol. Large doses of quinine and tincture of chloride of iron may be given in the hope that they will combat sepsis, but if the iron disturbs the stomach it must be discontinued. Inhalations of turpentine, creosote, and carbolic acid have been recommended. They may lessen the terrible stench created by the decomposition and perhaps soothe the irritated bronchi, but they cannot arrest the gangrenous process. For cough and pain morphine may be given, and it may likewise be administered when hemorrhage occurs.

For subacute or chronic gangrene such as occurs in diabetes or chronic tuberculosis, supportive treatment is indicated, together with the use

of stimulating inhalations, such as turpentine or oil of sandalwood. As to surgical treatment, it may be stated, as a rule, that operation is indicated early in every case in which a single limited lesion can be isolated, and the patient's condition is grave. If no alarming symptoms are present a little delay may be tolerated, but in any event the removal of a gangrenous focus would seem to be rational. If the lesion cannot be located, as will happen to the majority of cases, unless pulmonary destruction is extensive, exploratory incision may be made in an attempt to find the sphacelated mass. Empyema demands immediate operation. When small multiple foci are present operation is of no avail.

ABSCESS OF THE LUNG

Etiology.—Abscess of the lung is a term often applied indiscriminately to suppurative conditions of whatever type developing in that organ, although in many of them the lesion does not possess the characters of abscess in other viscera. This is due largely to the anatomical peculiarities of the lung and, although it gives rise to some discrepancy between clinical and pathological descriptions, practically the point is not one of extreme importance. Primary suppuration in the lung almost never occurs and consequently, although pus is found in the organ under varied circumstances, pulmonary abscess, properly so called, develops only in three groups of cases: (1) In areas of previously diseased lung tissue, (2) from plugging of a bronchus by a mass which may putrefy, and (3) as the result of the lodgment of infected emboli. In the first group are a number of conditions. Lobar pneumonia is occasionally followed by suppuration, the resulting abscess being either single and possibly occupying a large part of a lobe, or more often there are multiple smaller foci through the pneumonic area. This type is to be differentiated from a condition arising in pneumonia and commonly known as purulent infiltration, in which during resolution an excess of liquefied exudate macroscopically resembling pus, bathes the pulmonary tissue and gives rise to the name; microscopically and bacteriologically this material in such cases is shown not to be pus. In the nature of trauma with added infection, aspiration and deglutition pneumonias frequently produce suppuration by carrying pyogenic bacteria into the lung with food or other substances. The former is apt to occur after operations upon the mouth, tongue, or throat, or as a sequence of suppurative lesions of the upper respiratory passages. It occurs far more frequently after tonsillectomy than is commonly thought. Foreign bodies in the bronchi or lungs may be the cause of suppuration. Puncture of the pleura by an exploring needle or by a fragment of a broken rib or other body may be followed by pulmonary abscess. Emboli from whatever source, bearing pyogenic organisms and lodging in the lung, give rise to the so-called metastatic abscesses. These are usually small, nearly always multiple, and often extend to the pleura as cone-shaped areas, although abscesses may arise without the formation of definite infarcts. If the abscess be superficial, pleurisy develops over it and

rupture into the pleural sac is not uncommon, the latter giving rise to empyema or possibly pyopneumothorax.

Other instances of suppuration in the lung, at times designated as pulmonary abscess, are those in which the organ is invaded by pus from contiguous structures. This may occur in localized empyema, from extension into the lung of cancer of neighboring tissues, in suppurative lesions of the mediastinum, and in cases of pus formation in the abdominal cavity, particularly hepatic abscess and suppurating echinococcus cyst of the liver, which reach the lung through the diaphragm. In most of these cases the pus passes through the lung, gains access to a bronchus, and is expectorated instead of increasing locally by peripheral extension of the necrotic process and thus forming a true abscess. Extension by the lymphatics in these cases may, however, give rise to new foci of pus formation. Another form of pulmonary suppuration in the shape of a single diffuse suppurative lymphangitis, peribronchial in location, is sometimes found postmortem, but is unrecognizable during life by physical signs. It is in those cases that the use of the roentgen-rays in diagnosis is invaluable. In this the pus, which is found in the interstitial structure and larger lymphatic tracts, may be due to infection of the lymphatics by bacteria from the pleura or from the tissues around the root of the lung. Suppuration occurring in a tuberculous cavity as the result of secondary infection is sometimes designated pulmonary abscess.

Morbid Anatomy.—Abscess of the lung may be large or small, the size of a lobe or 2 cm. or less in diameter. The cavity contains the ordinary constituents of pus and usually in addition fragments of lung tissue and the remains of partially disintegrated alveolar epithelial cells. Fragments of lung in the form of alveolar elastica appearing in the sputum form a valuable aid in the diagnosis of abscess. The cavity of the acute abscess is bounded by a wall consisting of an inner layer of necrotic lung tissue containing polynuclear leukocytes, a second zone densely infiltrated with inflammatory products, and possibly containing proliferated connective-tissue cells, and a peripheral zone of cedematous pulmonary tissue. In some cases of high tissue resistance and slow progress of the abscess a limiting wall of new fibrous tissue is formed. If evacuation of the contents is complete, cicatrization of the entire area may take place. Neither of these terminations is common. The wall of a pulmonary abscess may become gangrenous, especially if the pus has been evacuated and the resulting cavity imperfectly drained. If the abscess wall be formed partly by the pleura, as is usual in embolic abscesses, the latter structure will be surmounted by a fibrinous exudate in which pus formation may or may not occur.

Symptoms.—The symptoms of suppuration in the lung vary somewhat in accordance with the cause of the development and the size and number of the lesions present. When due to a septic embolus, as in the course of septicopyemia, or one of the more malignant acute infectious fevers, as variola, symptoms of respiratory disturbance may be masked by the general constitutional manifestations of the disease. In other cases, however, cough, dyspnoea, pain in the chest, and the expectoration of

purulent sputum will be superadded to the other manifestations, provided that the patient does not succumb early to his general infection.

Abscesses due to the inspiration of *foreign bodies* are characterized by a septic temperature, cough, dyspnœa, and pain, a syndrome which may be said to characterize all forms of acute pulmonary suppuration; however, in this class of cases, it supervenes shortly after the foreign substance has lodged in the lung and is not superimposed upon another symptom-complex. Foreign bodies of vegetable nature, especially peanuts, usually set up an acute suppurative process. Septic foreign bodies induce suppuration rapidly.

When suppuration of the lung occurs in lobar pneumonia, its presence will be marked by continuation of the fever beyond the usual duration and failure of the consolidated areas to undergo resolution. The temperature may assume a higher elevation than that at which it was maintained during the course of the disease, but it will usually be characterized by fluctuations, assuming a distinct septic type with morning remissions and evening exacerbations. Dulness persists over the affected area and bronchial breathing or indistinct breath sounds will be heard on auscultation. As the morbid process advances and more tissue undergoes liquefaction, and especially after the abscess begins to empty itself, the signs of cavity in the lung may become apparent; amphoric breathing and coarse crepitant or bubbling rales may then be heard.

The sputum undergoes important changes, becoming grass-green, or sometimes dark brown in color. As soon as the abscess communicates with a bronchus its contents will begin to be freely discharged. Sometimes a gush of pus, so profuse as to fill the patients' mouth and nearly choke him, will suddenly occur. Fragments of elastic tissue are brought up with the expectorated material. The odor of the expectoration is not so foul as in putrid bronchitis and gangrene of the lung.

Not only do these changes in the objective symptoms take place, but alterations in the subjective symptoms may likewise occur. It not uncommonly happens, when a single large abscess has emptied itself in the manner just described, that the fever subsides and the general condition improves, although pus may be discharged for an indefinite period of weeks, months or years; some fever may also persist. The duration of the symptoms depend upon the rapidity with which the abscess becomes obliterated.

In another class of cases due to pneumonia, defervescence takes place in the regular manner, but in the course of two or three weeks the patient develops irregular fever, cough, and dyspnœa, and after being ill for some time may either begin to expectorate purulent sputum, or be seized with a violent paroxysm of cough and bring up a considerable quantity of pus. This is observed in some cases after tonsillectomy. Relief may then follow and healing take place, or the abscess fill again, and similar attacks follow. Sometimes the patient enters upon a period of decline, loses weight, runs a hectic fever, and succumbs to sepsis.

The minute abscesses occasionally formed seldom produce any symptoms. This is likewise the case with those small areas of suppuration which form around new growths, although they may be responsible for

the slight elevations and irregularities of temperature which sometimes occur. These small abscesses are frequently not suspected during life but are discovered at autopsy. The softening and liquefaction of indurated areas of lung tissue which sometimes occur in chronic fibrosis of the lung, do not give rise to the symptoms above described. Acute symptoms are not present, nor is the sputum characterized by the admixture of pure pus.

Complications.—When a pulmonary abscess is superficial, pleurisy almost invariably results and is very apt to be purulent. The abscess may also break through the pleura and cause empyema in this manner or perhaps give rise to pyopneumothorax. Purulent pericarditis and cerebral abscess are also occasional complications. The suppurative process may also terminate in gangrene. In chronic abscess cavities there is danger of hemorrhage taking place from erosion of vessels in the wall. Amyloid disease may supervene in chronic cases.

Diagnosis.—This may be very difficult. Small multiple pyemic abscesses may not produce distinct symptoms because of the violent disturbance caused by the general infection. When one or more large abscesses communicate with a bronchus so that pus gushes up and fragments of lung tissue are expectorated, diagnosis is assured. The finding of elastic tissue is an infallible sign and will remove any doubt which may have previously existed although the presence of tubercle bacilli may prove it to be a tuberculous cavity. When defervescence in lobar pneumonia is atypical or retarded, or when chills and irregular fever occur after crisis has taken place, suspicion should be aroused as to the possibility of suppuration in the lung although empyema is a much more common cause. If the sputum undergoes the characteristic changes, the suspicion will be strengthened and probably confirmed in course of time by rupture of the abscess.

The principal conditions with which abscess of the lung might be confounded are bronchiectasis and empyema. The former, although presenting some symptoms common to abscess, such as the expectoration of purulent sputum and hectic temperature, is to be differentiated by the history and absence of elastic tissue in the expectoration.

In purulent pleural effusion which has ruptured into the lung the physical signs of the primary disease usually remain, so that dulness over the posterior pulmonary area increasing from above downward will be present with diminished breath sounds over this area. In some cases the symptoms and signs of pyopneumothorax supervene.

Diagnosis between an interlobar empyema and a pulmonary abscess which has not communicated with a bronchus is practically impossible except by the aid of the roentgen-rays and even after perforation of the one and rupture of the other has occurred there may be nothing by which a differential diagnosis can be made. It may be impossible to distinguish abscess from gangrene affecting a limited area of pulmonary tissue, although offensive odor of the breath and foul-smelling expectoration suggest gangrene.

Prognosis. Pulmonary abscess is a serious disease, but the prognosis depends in some degree at least upon the cause and upon the size and

number of lesions present. Acute multiple abscesses due to septic emboli are always fatal. Abscesses due to penetrating wounds usually heal readily unless a large area of tissue has been destroyed. In single abscess following lobar pneumonia hope for recovery should always be entertained. If the abscess ruptures, or can be evacuated by surgical intervention either by bronchoscopy or external methods there is a fair prospect of recovery. The longer the abscess cavity persists the greater is the danger of death from septic poisoning and exhaustion, from amyloid disease, and from hemorrhage due to erosion of vessels in the abscess wall. When a suppurative process involves a lymph node it is remarkable how often recovery occurs by its rupture into a bronchus.

Purulent pericarditis and rupture into the pleural cavity render the prognosis more unfavorable. If surgical intervention can be practised at once in the latter occurrence the patient's chances of recovery will probably be increased, but unless operation is done at once, they are certainly diminished.

Treatment.—Medicinal treatment must be directed mainly to sustaining the patient's strength. Alcohol should be given freely. Nutritious liquid food must also be supplied. Inhalations of phenol have been highly recommended, but it is doubtful if they accomplish any good. In chronic abscess, iron and arsenic in addition to alcohol will be found useful. It is in this class of cases, too, that antiseptic inhalations may relieve associated bronchitis. Phenol, creosote, eucalyptol, and benzoin may be tried. For excessive cough small doses of opium or codeine are permissible, but care must be taken not to give enough to check the secretions or to so benumb the patient that if the abscess ruptures he will fail to cough up the pus.

In small multiple pyemic abscesses treatment is of no avail. In regard to the surgical treatment of pulmonary abscess, whenever an abscess can be located, and there is reason to believe that other foci of suppuration are not present, the pus should be evacuated by the aid of the bronchoscope or external pneumotomy should be performed. Although some pneumonic abscesses heal spontaneously after rupture occurs, it seems that they should be opened and drained if bronchoscopic treatment is not effectual. By treating them in this manner the patient will be less exposed to such complications as empyema, purulent pericardial effusion, cerebral abscess, and septicopyemia. When due to extension of suppuration processes originating outside the lung, for instance, to rupture of a subphrenic abscess or an empyema, operation is also urgently demanded. So likewise is it when an abscess breaks into the pleural cavity.

NEW GROWTHS OF THE LUNG

Etiology.—The etiology of primary tumors of the lung is enveloped in the mystery which surrounds that of new growths in general. Primary cancer is much more frequent, 3 to 1, in men, and of West's 6 cases of primary sarcoma 5 were in men, the sex in the other case not being stated. This by inference is in harmony with Aufrecht's belief that trauma is of etiologic importance. In each of his 4 cases of cancer there was a

clear history of injury, and he cites similar instances from the experience of others. Workers in cobalt mines appear especially predisposed to pulmonary cancer.

Morbid Anatomy.—This depends largely upon whether the growth is benign or malignant, primary or secondary. In general, primary tumors are much less frequent than secondary, due either to metastasis or to extension from contiguous tissues. In 20,160 autopsies, Wolff found 46 primary tumors of the lung. The primary are commonly unilateral, the secondary bilateral. The latter, when metastatic in origin, are often widely disseminated.

Benign tumors of the lung are very rare. Adenomata originating in the bronchial glands have been found. Of the connective-tissue series, osteoma, chondroma, fibroma, and lipoma are occasionally met; they are usually small and multiple. A true primary osteoma was reported by Virchow, but there seems little doubt that some so designated have been in reality calcific foci in tuberculous or other disease areas. A few cases of primary enchondroma are on record. They are small, multiple tumors originating from the bronchial cartilages, rarely exceed 1 cm. in diameter, give rise to no symptoms, and consequently are of pathological interest only. Of secondary osteoma and chondroma, 14 cases are on record. Fibroma is rare, as is also lipoma.

Malignant tumors are sarcomas and carcinomas but the latter are by far the more common. In Adler's statistics there were 374 cases of primary carcinoma and 94 of sarcoma. The *sarcoma* is relatively rare as a primary tumor. Of West's 16 cases of sarcoma of the lung, 6 were primary in that organ. The endothelioma, or sarcoma derived from endothelial cells, is the most common primary malignant connective-tissue tumor. It usually originates in the pleura, but may spring from the lining cells of trabecular lymph spaces or bloodvessels. Of sarcomas, secondary in the lung, those originating in bone are the most frequent, a third or more coming from this source. So far as the lung is concerned these tumors do not always conform to the general rule regarding age, and appear more often in adult or advanced life. In some cases there is a long interval between the appearance or removal of the primary tumor and the metastasis in the lung. Prentiss reports a case of removal of a sarcoma of the testicle with symptoms of secondary growth in the lung developing four years later, the patient living another year. Melanotic sarcomas also appear. Possibly belonging to this tumor group is the syncytioma, which occasionally develops in the lung as a secondary growth. Hypernephroma is a frequent source of metastases in the lung.

While primary *carcinoma* is more frequent than sarcoma, the greater number of cancers are secondary. The primary is commonly encephaloid in type, although from the anatomy of the lung most secondary growths also, even if from a scirrhus, assume a very cellular structure. West particularly emphasizes the fact that cancer of the root of the lung tends to become excessively fibrous. When primary the tumors may involve most or all of a lobe or an entire lung. Secondary foci may develop by dissemination of the original tumor. Perl, Mallassez, Boix, and others,

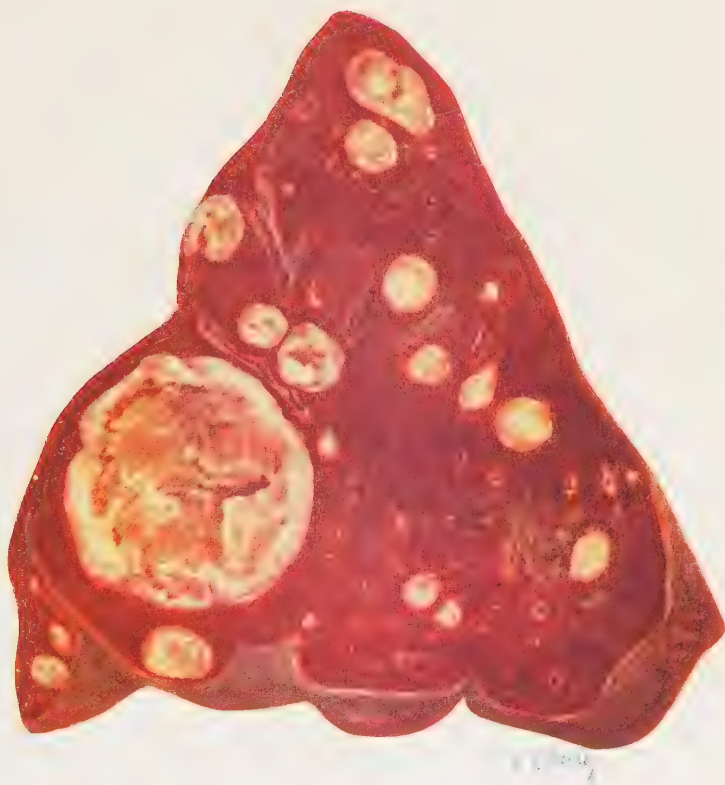
endorsed by Aufrecht, hold that true primary cancers of the lung take origin from the alveolar epithelium. The pulmonary tissue may be invaded, however, by tumors originating in bronchial mucous glands. Primary cancer may remain in the lung or extend to neighboring structures, including the opposite lung. The tumor may appear externally, but extension through the chest wall is not frequent. At times when a bronchus is invaded, the growth extends through the wall and appears as papillary masses projecting into the lumen. In these cases, possibly more often than when the growth is confined to the pulmonary alveoli, fragments or individual cells may be detached and expectorated; a few cases have been diagnosed by finding these in the sputum.

Secondary cancer of the lung is commonly bilateral unless due to extension from contiguous tissues, these including the mediastinum, neck, chest wall, and through the diaphragm from abdominal structures. The possibility of extension from the parietal pleura without the intervention of adhesions is held by some writers. Metastasis by the lymphatics is a common source of these tumors, but cells are also brought to the lungs by bloodvessels. The latter method may give rise to relatively few small or large nodules in the interior and appearing as bossed or umbilicated elevations beneath the pleura, or to innumerable small, scattered foci; to the latter condition the term *carcinosis* of the lung has been applied. Cases of extension to the lung through the air passages of squamous epithelioma of the mouth or larynx have been observed.

The effect on the lung of all the varieties of malignant growths is much the same. According to their size they are substituted for a small or large part of the pulmonary tissue and exert pressure on all or a part of the remainder. The latter usually leads to compression and atelectasis of the tissue immediately bordering the tumor nodules, although as a whole the intervening lung, especially if the growth be extensive in the shape of multiple foci, is *emphysematous*. If the tumor affects a lobe or more as a single large mass, the remainder of the organ is sure to become overdistended. Congestion and possibly added oedema may occur in the pulmonary tissue surrounding the tumor nodules; under these circumstances *hemoptysis* not infrequently results. Subacute inflammatory changes may also take place in the bordering tissue and in some instances lead to softening; in addition to or independent of this, the tumor itself may soften, the process in either instance resulting in cavity formation. Pressure on the blood and lymph vessels and on the bronchi by tumors at the root of the lung leads to secondary changes, as atrophy, necrosis, oedema, and atelectasis, such as would develop from like interference by other causes. *Hydrothorax* or *pleurisy*, the latter either serofibrinous or hemorrhagic, not infrequently complicates cancer or other malignant tumor of the lung.

Symptoms.—The benign tumors may be disregarded because of their rarity and also for the reason that when they are present they may not produce any disturbance. As carcinoma and sarcoma give rise to the same symptoms they may be considered together. When these growths are secondary it sometimes happens that their evolution is so slow and manifestations of malignant disease in other parts of the body so pro-

PLATE III



Secondary Sarcoma of Lung.

nounced that evidence of pulmonary involvement is not detected during life, the lesions being discovered only upon autopsy. As a rule, however, especially when the tumors are primary, the disease manifests itself by marked, although by no means distinctive, symptoms consisting primarily of dyspnœa, cough, and expectoration.

Dyspnœa is constant and progressive. At first perhaps only of slight degree or noticeable upon unusual exertion, it gradually becomes worse until in extreme cases it may amount to orthopnœa. It is especially severe in cases in which the neoplasm invades the mediastinum and presses upon the lower portion of the trachea and the great vessels. Interference with the circulatory area of the lung, invasion of the bronchi, and a pleural effusion all contribute to its production, but it is of course most intense when the trachea is compressed. Tumors which grow rapidly naturally produce dyspnœa more quickly than do those whose evolution is more gradual. Cough is variable, depending somewhat upon the size and location of the growth. Thus when a tumor is so situated as to compress the pneumogastric nerve the cough will be hard and dry, whereas if the tumor is disintegrating, or if an associated pneumonia be present, it will be freer and accompanied by expectoration.

Expectoration is variable both as to its quantity and characteristics. The sputum may remain mucoid or mucopurulent throughout the course, although it is often blood-stained, and has also been known to be of a bright green color. Sometimes it is coughed up as clear red, homogeneous masses, which have been compared to currant jelly. There is nothing significant about this sputum; it is merely a homogeneous admixture of mucus and blood, the two being so thoroughly blended that they cannot be distinguished. Sometimes a little pure blood may be coughed up, and if the neoplasm extends into a large air cavity, free hemorrhage may result. Particles of the tumor itself may also be expectorated. Hampeln called attention to the presence in the sputum of unpigmented polymorphous cells of different sizes in which both nuclei and nucleoli show plainly. He believes that these cells are pathognomonic of cancer.

Intercostal *pain* is not uncommon, but it may not be so severe as to cause much distress. In other cases it is atrocious. West mentions a case in which neuralgic pain extended down the inner side of the arm, being due to pressure upon the outer costohumeral nerve. Herpes zoster sometimes runs along the course of a nerve thus compressed. When the pleura is involved intense pain may be a constant symptom. Other symptoms worthy of mention are, fever, hemoptysis, dysphagia, interference with phonation, and disturbances of the circulation. Fever is present in some cases, and Fränkel observed it in 19 out of 35 cases. It no doubt is often due to associated suppurative processes in the lung, but it also has been attributed to resorption of the tumor elements.

Pressure of the growth upon the œsophagus causes dysphagia. If the recurrent laryngeal nerves be compressed, disturbances of phonation such as hoarseness, inspiratory stridor, and aphonia will result; pneumogastric compression may cause cardiac disturbance, such as irregularity. Pressure upon the sympathetic will give rise to inequality of the pupils

and flushing of one side of the face. If the growth encroaches upon the large bloodvessels in the lung, circulatory disturbances are produced. If the vena cava is involved, pleural effusion is likely to supervene.

In regard to cachexia, it may be stated as a rule that it develops more slowly and is not so pronounced in primary malignant disease of the lungs as it is in other forms of cancer and sarcoma.

Physical Signs.—These depend upon the size and situation and upon the condition of the surrounding pulmonary and other contiguous tissues. Thus, when a considerable area of lung is involved by an extensive infiltrating mass the signs will be different than when only a few small, isolated nodules are present. Again, when bloodvessels are compressed or elevated by the neoplasm, manifestations on the part of the circulatory system will be observed which are absent when the tumor is so situated as not to impinge upon the vessels.

Upon inspection, changes in the shape of the thorax may be noticed. In case there is a large infiltrating growth in the lung the corresponding side of the chest may bulge out and the intercostal spaces be widened. A pleural effusion may also cause bulging. On the other hand, when collapse of the lung has taken place as the result of bronchial occlusion, the thorax may be retracted and its circular measurement considerably diminished. The affected side does not move with respiration.

When the neoplasm presses upon the superior vena cava, considerable distention of the superficial cervical veins will be seen. If the pleura is involved so that the calibre of the internal mammary vein is diminished by compression, the superficial veins of the chest will be unduly filled and stand out prominently under the skin. This is an important sign.

Palpation shows that vocal fremitus is normal or exaggerated according as the growth is localized or diffuse. Percussion elicits variable sounds which depend upon the extent and character of the neoplasm and the condition of the parts around it. In diffuse infiltration of the lung, dullness may be elicited over a considerable area. Areas of atelectasis as well as patches of pneumonic infiltrate around a softening and isolated nodule near the periphery of the lung also may give a dull note. As a rule, isolated nodules in the early stages of their evolution do not cause any changes in the percussion note. Sometimes resonance is slightly impaired or a hyperresonant note may be obtained. Hyperresonance is often heard when a bronchus becomes obstructed; when a cavity is formed by disintegration of the neoplasm and inflammatory softening of adjacent tissue, an amphoric note is obtained over the cavity.

The results of auscultation are likewise variable. In extensive infiltration the breath sounds are much diminished, or may be absent; sometimes they are replaced by bronchial breathing. In the nodular form of the disease, however, very slight alterations will be detected. The breath sounds may be somewhat diminished in intensity and perhaps a little rough. Associated pulmonary congestion or oedema, as well as bronchitis, give rise to rales of various kinds. In case a cavity is present cavernous breathing and pectoriloquy may be heard. The cardiac sounds are often abnormally distinct, being transmitted through areas of solidified tissue.

Complications.—The chief complications are pleurisy, pneumonia, gangrene, and atelectasis. The pleura may be attacked by the malignant growth and becomes much thickened and indurated. Effusion into the pleural cavity is not uncommon when such involvement is present, and the fluid is very likely to be sanguinolent. Rarely, a purulent effusion may be present. Pneumonic consolidation and œdema of the lung are sometimes observed, the latter no doubt is in many instances due to pressure of the growth upon the pulmonary veins, although it may result from stasis in the smaller vessels. Gangrene may ensue either as a result of the destructive process itself or may follow occlusion of bloodvessels by the pressure of the neoplasm upon them. Atelectasis is not uncommon, owing to occlusion of the bronchi. Metastases in other parts of the body—the liver, kidneys, and joints—sometimes occur. Distinct enlargement of the supraclavicular glands may be noticed.

A very few cases have been reported in which a cancer of the lung has perforated externally, but such an occurrence is exceedingly rare.

Diagnosis.—This may be very difficult if the tumor is small and situated deep in the lung. Here again the roentgen-ray is invaluable. Even when several such isolated nodules exist, characteristic symptoms may not be manifested and the physical signs may be similar or identical with those in other pulmonary disorders. Metastatic growths are very liable to escape attention, especially if they occur late in the course of the primary malignant disease. Pulmonary symptoms associated with emaciation and cachexia, supervening after the removal of a malignant growth in another part of the body would naturally arouse suspicion.

In other cases where the malignant process is extensive and contiguous, and perhaps even remote structures are involved, diagnosis will be readily made. A combination of such characteristic phenomena as dyspnœa unassociated with cardiac disease or severe bronchitis, mediastinal compression, enlargement of the supraclavicular glands, expectoration of currant-jelly sputum, together with the physical signs of pulmonary consolidation or excavation, will leave little or no doubt as to the nature of the affection with which we have to do. The finding of particles of tumor in the sputum makes the diagnosis positive.

Cases in which there is early involvement of the pleura may be most difficult to recognize. Bulging of the thoracic wall may be caused either by a tumor or by an accumulation of fluid in the pleural cavity, but when due to the former cause the tumefaction is apt to be more irregular than when it results from the latter. An encysted empyema, however, might give rise to a localized bulging in the side, and is therefore to be borne in mind. In tumor the dulness may extend from above downward, a condition quite the reverse of that which obtains in pleural effusion. In tumor, moreover, dulness is often not uniform in different parts of the chest, whereas in pleurisy with effusion there is little variation in its degree of intensity unless the patient changes his position.

Thoracentesis affords valuable aid. In some cases the exploring needle may be carried through a much thickened pleura and then fail to withdraw any fluid; this points strongly to malignant disease, and even though fluid finally be reached the thickening is suggestive of malig-

nancy. If shreds of tissue which adhere to the exploring needle prove to contain carcinomatous or sarcomatous cells, the suspicion is converted into positive knowledge. When fluid is obtained its character may elucidate the nature of the malady; in malignant disease it is apt to be hemorrhagic. The presence of a sanguinolent effusion, however, is not of itself conclusive evidence of malignant disease, for it sometimes occurs in tuberculosis and renal disease and when a previous tapping has been done. The presence of cancerous elements in the effusion is conclusive.

Neoplasms of the lung which produce mediastinal compression may give rise to symptoms, some of which are identical with those produced by aneurism of the aorta. When a tumor is so situated as to elevate the great vessels distinct pulsation may be felt, and circulatory disturbances may also be produced. The most valuable point of differential diagnosis is constituted by the fact that when an aneurism attains sufficient size to produce symptoms it will form an expansile, pulsating tumor. Over this pulsating area a dull percussion note is found. In aneurism there is no enlargement of the supraclavicular glands, and changes in the sputum such as may occur in malignant disease of the lung are not present. The fluoroscopic examination is frequently of great assistance. A new growth does not show the expansile pulsation of an aneurism. A history of syphilis indicates aneurism but in some cases the tumor may be a gumma.

New growths of the lung may be confused with tuberculosis. Thus when a few small, isolated, primary nodules undergo softening, with the result that cavities are formed and hemorrhage takes place owing to erosion of vessels, the disease may be mistaken for pulmonary tuberculosis. If a small hyperresonant area be discovered in the upper anterior region of the thorax, the error is likely to be more firmly fixed in the physician's mind. The presence of fever in such cases lends aid to the mistake, as does likewise the existence of rales produced by inflammation around the area of disintegrating tissue. In such cases the age affords some assistance. Such hemorrhage in a person past middle life should direct attention to the possibility of neoplasm. In malignant disease, enlargement of the supraclavicular lymph glands may be found, whereas in tuberculosis their size will probably not be increased. Examination of the sputum will in course of time decide the question.

Prognosis.—Malignant disease of the lung is of course incurable. Death may result from asthenia, asphyxia, hemorrhage, gangrene, or œdema. In regard to the duration of life no adequate data are obtainable, for the reason that there is no way of determining at what time the disease begins. Some patients die within a few weeks or months after the first manifestation of symptoms. Others may live for a year or two.

Treatment.—All that can be done is to relieve symptoms and endeavor to sustain the patient's strength. Morphia and cannabis indica should be used freely to control pain. Oxygen may be administered for dyspnœa, but when the latter is excessive and due to compression of the trachea, little good can be expected to follow its use. Operative treatment offers no hope of success. If a primary growth could be recognized early it might be successfully removed, provided it were small; but it is rare to

make a diagnosis sufficiently early to enable us to entertain any thought of surgical intervention. Treatment by the roentgen-rays is palliative and retards the progress of the disease in some cases.

COLLAPSE OF THE LUNG.

Postoperative and posttraumatic pulmonary collapse has very properly received much attention during and since the World War. It is a form of atelectasis. Often it involves a very large part of the lungs and without doubt many patients have been and are thought to be cases of postoperative pneumonia when in reality collapse is present. The condition was first emphasized by W. Pasteur in 1890¹ in cases of post-diphtheritic paralysis of the diaphragm, but as long ago as 1876 Pearson-Irvine reported a condition which was identical. W. Pasteur's most important contributions were in his Bradshaw Lecture in 1908 and again in 1914.² Since then J. Rose Bradford³ has repeatedly written on this topic, most of his observations being made in military practice. A very considerable number of contributions are in the literature. One of the most recent and thorough is that by W. E. Lee.⁴

The collapse may involve both lungs or be limited to one lobe, usually a lower lobe, and interference with the action of the diaphragm is without doubt an important factor in its induction. The presence of a foreign body which completely plugs a bronchus results in collapse of the area of lung supplied by it. In some cases a plug of tenacious mucus has the same effect. When the onset is sudden, in from a few hours to several days after the exciting cause, there may be a fever as high as 104° F., and the respiratory rate is markedly increased for obvious reasons. Both of these features resemble lobar pneumonia. Important physical signs are immobility of the affected side and displacement of the apex beat toward the affected side in distinction from the displacement in pleural effusion. If, however, the lesion is bilateral, the apex beat may not be altered as to location. The intercostal spaces are narrowed, not widened as in effusion, but the resemblance to pneumonia is again to the fore by virtue of the fact that percussion gives dullness or even flatness. Pectoriloquy is often marked, but breath sounds and fremitus are not absent. Rales may develop after some hours or days and a pleural friction rub may be present, thereby presenting more signs commonly attributed to pleurisy or pneumonia and this point is again emphasized by the fact that more or less profuse expectoration may come on as the process of resolution takes place, for an inflammatory process is practically always an associated condition. Bradford states that when the left side of the chest is affected the lower part of the thorax instead of being dull is hyperresonant because the diaphragm is pulled upward, and it may be that some of this resonance is due to gas in the stomach or splenic flexure.

¹ *International Journal of Medical Science*, 1890.

² *British Journal of Surgery*, 1914, vol. i.

³ *Quarterly Journal of Medicine*, 1918-1919.

⁴ *Progressive Medicine*, December, 1922.

This hyperresonance is not found on the right side because the liver follows the diaphragm as it rises. The degree of dyspnœa depends almost entirely upon the degree of the collapse. The use of the roentgen-rays is an invaluable aid in diagnosis. Prognosis depends upon the cause and the general state of the patient and the degree of collapse. In the average case it is very good if complications do not ensue.

Pulmonary collapse is to be avoided in operations on the abdominal area by resorting to the Trendelenburg position for as short a time as possible, particularly in obese and feeble patients. After operation the Fowler position is advantageous as a prophylactic measure. In any event a marked dorsal decubitus is to be prevented if possible. Deep respirations, after the patient recovers from the anesthetic, are also prophylactic and perhaps even curative.

In case of a foreign body or tenacious mucus plugging a bronchus, removal by bronchoscopy is indicated. Beyond these measures there is no therapy save that based on general principles.

CHAPTER VII

PNEUMOCONIOSIS

By H. R. M. LANDIS, M.D.

THE term "pneumoconiosis" is applied to respiratory affections which develop as the result of the inhalation of inorganic dust. In 1828 Stratton suggested the term anthracosis to designate the changes produced by the inhalation of dust. The term pneumoconiosis was introduced later by Zenker to indicate all forms of dust infection. This is the preferable term, although it is a common practice to refer to the particular type of dust under a specific heading, as anthracosis (coal), siderosis (iron), silicosis (silica), etc. In addition, respiratory conditions due to the inhalation of dust are often popularly referred to as miners' asthma, miners' consumption, grinders' rot, potters' asthma or rot, etc.

Dating from the time of Ramazzini's book "On the Diseases of Tradesmen" (*De Morbis Artificum Diatriba*), two and a quarter centuries ago, it has been known that workmen, if exposed constantly to dust, develop serious respiratory disorders. During the past seventy-five years, the literature on the dangers of dust inhalation has reached voluminous proportions. In spite of this, however, pneumoconiosis, until very recently never gained a place in the morbidity and mortality returns.

Possessed of an exact etiology, a clear-cut pathology and a quite definite symptomatology, the condition is rarely referred to under its own appellation. Individuals with pneumoconiosis are almost invariably referred to as having tuberculosis, asthma, chronic bronchitis or pleurisy, partly because of the similarity of symptoms and partly because at some time during the course of the disease these conditions may develop but they are always secondary.

With the ever-increasing interest in diseases resulting from industrial hazards and the introduction of the roentgen-rays in the study of pulmonary conditions, the recognition of pneumoconiosis is becoming more and more prevalent. In the future it is certain that it will be referred to more under its own name.

Etiology.—Although there is not the least uncertainty as to the evil effects of the inhalation of certain types of dust, there is still too much confusion as to the relation of dust in general in the causation of pneumoconiosis. It has not been until the past decade that any attempt has been made to distinguish between the various forms of dust. Even today writers are apt to class as dangerous all occupations in which dust occurs, irrespective of the dust involved. A number of years of study of this subject have convinced me that the only type of dust involved in the production of pneumoconiosis is the inorganic form. It is generally accepted that any of the inorganic dusts will produce pneumoconiosis,

providing the exposure is sufficiently long and sufficiently intense. Inorganic dusts vary, however, in their ability to cause damage. The inhalation of pure silica dust leads very rapidly to serious changes in the respiratory tract. This dust is most often encountered in mining operations and is a serious industrial hazard in the gold mines of South Africa, and in the zinc, copper, and some coal mines of this country. Pure silica is also encountered in some of the industries, notably in potteries. In the pottery industry, however, only a few of the workmen are exposed to pure silica. The majority are exposed to the prepared clay, containing a small amount of silica, used in the manufacture of china, and as a result the irritating effects are of much slower evolution. Pure silica produces crippling effects in from six to eight years, while clay dust mixed with silica rarely incapacitates the worker in less than twenty to twenty-five years.

Next to silica, coal dust, notably the anthracite form, is the most common source of pneumoconiosis. In the anthracite mines a pneumoconiosis is inevitable if the worker follows the occupation long enough. Marked symptoms usually develop in from twenty to thirty years of such employment. Anthracosis in a mild form is a common finding in the lungs of all urban dwellers. In manufacturing centres, where the air is heavily laden with soot, the lungs may become almost black. This form rarely gives rise to symptoms. In some of the anthracite mines, rock-blasting adds to the seriousness of the hazard, and as a result the fibrosis is always a more marked feature.

Some forms of inorganic dust, notably cement dust, lime dust, plaster of Paris, etc., are believed to be innocuous. In the case of cement dust, the industry is of too recent origin to draw definite conclusions. It is recognized that dusts of this form are relatively non-irritant and that years must elapse before marked changes are produced in the lungs. There are some who would exempt all forms of inorganic dust except silica. It is their belief that it is the silica content in the dust that is important and that inorganic dust free from this element produces no damage. From a practical viewpoint the essential fact to keep in mind is that a worker exposed to any form of inorganic dust is likely to show roentgen-ray evidences of a pneumoconiosis.

Organic dust, on the other hand, plays no part whatever in the production of pneumoconiosis. It is important to bear this in mind. In a study of 50 autopsy protocols, relating to individuals who had been exposed to organic material, I did not find the slightest evidence of changes which characterize lungs exposed to the inorganic form. This confirms the experience of Pancoast and myself in a roentgen-ray study of a similar group of workers.

When a worker employed in an industry dealing with organic material does show evidence of pneumoconiosis, an analysis of the dust will always show that it contains a high percentage of inorganic dust. For example, Drinker found that the respiratory symptoms among employees of a jute factory were not due, as was suspected, to the jute fibres, but to a high inorganic content. Pancoast and myself had in a similar experience in a carpet factory. In both instances, an analysis of the dust showed that it contained nearly 60 per cent. of inorganic material.

Of course organic dust may give rise to allergic phenomena and it is also possible that this dust may act as a carrier of bacteria. Neither of these, however, have anything to do with pneumoconiosis.

Pneumoconiosis and its Relation to Tuberculosis.—From the beginning of our knowledge of the evil effects of the inhalation of dust, the opinion has prevailed that it predisposed to tuberculosis. In the past much confusion has been caused by failure to recognize the presence of pneumoconiosis. Patients suffering from pure pneumoconiosis in the advanced stage show symptoms and physical signs differing but little from those in pulmonary tuberculosis. The result is that workers exposed to inorganic dust, particularly miners and potters, have been regarded, until recently, as having tuberculosis, and this attitude has been reflected in the popular names, such as miners' consumption, potters' phthisis, etc. It is to be borne in mind that while tuberculosis is a common complication in some forms of inorganic dust disease, it is not necessarily so. Pure, uncomplicated pneumoconiosis is of frequent occurrence.

At the same time, it is recognized that the rapidly developing types of pneumoconiosis, such as occur following exposure to pure or nearly pure silica, are often complicated by tuberculosis. On the other hand, anthracosis, and disease due to less irritant dusts, are believed by many to be a protection against tuberculosis but this, I believe, is still a debatable point. The White Haven Sanatorium, situated in the anthracite region, has had many miners as patients in a period of twenty-five years. In an analysis of these cases, the incidence of tuberculosis as a complication was entirely too high to warrant the belief that coal dust is a protective agent. It seems to be true that in the acute forms of pneumoconiosis (silicosis) acute or subacute forms of tuberculosis are not infrequent. On the other hand, in the slowly evolving type, as in potters, tuberculosis, when it occurs, is apt to be of the chronic, non-toxic form. This is true also of coal miners. The reason for this is not altogether clear but it seems possible that in those cases in which silica is the dominant factor pneumoconiosis is rapidly produced and is in the nature of an acute or subacute inflammation. The less irritant forms of dust produce a very mild inflammatory reaction which is chronic and attended by very little local reaction. On this hypothesis it is conceivable that a lung acutely or subacutely inflamed becomes a fertile field for the tubercle bacillus, which can grow readily, and equally readily the infection may spread. In the chronic forms, with the formation of fibrous tissue almost from the beginning, the lung offers an unsuitable site for the development of the tubercle bacillus. While it may, and often does, lodge in such lungs, it tends to localize and gives rise to relatively slight toxic symptoms.

Other hypotheses are suggested by Mavrogordato,¹ by Gye and Kettle² and by Collis.³ Mavrogordato believes that the tuberculous process spreads rapidly in the silicotic lung because it invades the thin-walled new bloodvessels, which have formed as the result of the cutting-off of the original vessels by the fibrosis of the perivascular lymphatics, and the

¹ *Publications of the South African Institute for Medical Research*, March 31, 1922, No. 15.

² *Lancet*, 1922, ii, 855.

³ *Public Health*, London, 1914-15, vol. 28.

new vessels have not developed normal defenses. Gye and Kettle ascribe the frequent association of tuberculosis and silicosis (1) to the destructive action of the silica on the cells, causing necrosis, in which the tubercle bacilli multiply, and (2) to the disorganization of the lymphatic drainage of the lungs. Collis suggests that pure silica is readily confined to colloidal compounds which poison the cells and render them vulnerable to the tubercle bacillus.

This much is certain—the tubercle bacillus has nothing to do with the creation of the condition known as pneumoconiosis. The latter may or may not be a factor in rendering the individual susceptible to tuberculosis, but it is a distinct entity, and unless individuals so affected are exposed to the tubercle bacillus, they would never develop tuberculosis. The opportunity for such infection is nearly always present, especially in the case of mine workers. The dark and poorly ventilated mine offers every opportunity for the tubercle bacillus to live for an indefinite time. Then too, as Lanza has shown in a study of the zinc miners, the hygienic conditions of the homes often offer ample opportunity for infection.

Pathology.—The essential pathological feature of pneumoconiosis is a fibrosis, brought about by the deposition of dust particles in the lungs which, acting as any other foreign body, produce an inflammatory reaction. This in turn leads to the formation of fibroid tissue.

The protective mechanism in the upper air tract (moisture and the action of the ciliated epithelium lining the trachea) are effective against organic dust and to some extent against many forms of inorganic dust particles. Silica, however, is rarely arrested except for a brief period. Mouth-breathers have been said to be more susceptible, but this has not been proved. An excess of lymphoid tissue or defects (deviated septum, chronic rhinitis, etc.), are said to increase the susceptibility. Once the dust passes the primary defenses, it reaches the alveoli and the pathology of pneumoconiosis begins.

When the dust particles enter the alveoli, they set up a catarrhal process, with the proliferation of a certain type of cells, which have been termed “dust cells.” There is some question as to the exact origin of these cells, namely, as to whether they should be classified as an alveolar epithelial cell, a mononuclear leukocyte or an endothelial cell. An analysis of the evidence as to the origin of the “dust cells” favors the view that they are endothelial in character. The “dust cells” produce two essential changes, first, and foremost, fibrosis, and second, blockage of the lymph channels. Silica, above all the dusts, seems to possess the faculty of protecting the dust cells from autolysis and lymph digestion, so that they can accumulate in and block the lymphatics. Other dusts, such as coal, are destroyed and do not block the lymphatics. The difference is said to lie in the fact that silica particles are slightly soluble in alkaline juices, and that an alkaline silicate is precipitated, which preserves the cells.

With coal dust, cement dust, or other dusts which cause fibroid changes and moderate silica inhalation, the lymph channels do not become blocked. The lymph flow is maintained toward the hilum, and for thirty or forty years the individual may not show evidence of fibrosis beyond the first stage, or a nodular fibrosis only in those portions of the lungs where the

greater part of the inspired air goes, namely, the central portions. But if silica is inhaled in great quantities, widespread changes occur. Small fibroid nodules form and these increase in size and coalesce to form larger nodules from the size of a pinhead to that of a pea. It is the presence of these nodules that gives to the roentgen-ray film the characteristic picture of the second stage. In addition to the formation of these nodules, interstitial fibrosis continues to develop in the interalveolar septa and may involve the alveoli, bronchioles and vessels.

As time goes on, the fibroid changes become more and more marked. Large fibroid areas appear, and the lung as a whole becomes dense, inelastic and very resistant to cutting. Along the free margins and at the bases emphysematous areas may be prominent. As the result of this widespread fibrosis in the lungs, certain other changes occur. The pleura shares in the inflammatory process and the pleural cavities may be completely or in part obliterated by adhesions. In common with fibrosis of the lungs due to other causes, dilatation of the bronchi is commonly present in the third stage of the disease, and clubbing of the fingers is often noted associated with the dilatation of the bronchi.

The *diaphragm* plays an important part in the pathology of pneumoconiosis. The leaflets may show interstitial changes; the angles, especially the inner or pleuro-cardial angle, may be obliterated, and in addition the contour of the leaflets is commonly deformed in the advanced stages. All of these changes tend to restrict the action of the diaphragm and with the inability of the fibroid and inelastic lung to expand, lead to the dyspnoea which is such a common feature.

Although not properly a part of the pathology of pneumoconiosis, tuberculosis is so commonly associated with the process that it merits a brief comment. Tuberculosis, when it occurs, may assume any of its usual forms. The chronic ulcerative type with cavity formation is probably the most common. Certainly in potters this is the usual type, at least anatomically. Constitutionally it differs somewhat from uncomplicated tuberculosis, in that toxic or constitutional symptoms are slight, probably because of the extensive fibrosis already present. Miliary tuberculosis occasionally complicates the pneumoconiosis. The large fibroid areas that so often occur in the late stages of pneumoconiosis are regarded by some as the joint product of the dust cells and the tubercle bacillus. Many of these patients have no tubercle bacilli in the sputum, and the coexistence of the tuberculosis is only determined at autopsy or by histological studies.

Symptoms.—There is no symptom or group of symptoms characteristic of pneumoconiosis. Exposure to any form of dust, even for a brief period, is apt to cause some irritation of the upper respiratory tract, as manifested by a dry and unproductive cough. This is not always the case as many of the inorganic dusts, such as coal dust and that found in potteries, may cause no objective disturbance for years. On the other hand, fine silica may give rise to serious respiratory symptoms in so brief a period as two years if the exposure is sufficiently intense. The conditions under which the silica hazard is usually encountered will bring about symptoms in from six to eight years, while the more innocuous forms (coal, lime, cement, etc.) take from ten to thirty years or even longer.

The first *symptom*, as a rule, is a slight irritation in, and a desire to clear, the throat. Next, a morning cough appears, which later is accompanied by blackish, viscid sputum. As time goes on, the lung becomes the site of more and more dust and there is a corresponding increase in fibrous tissue. The worker then begins to experience some tightness in the chest. Shortness of breath also becomes more and more marked, which has given the popular names of "miners' asthma," etc. In some cases distinct pleuritic pain is an early symptom and may give rise to considerable discomfort. Until the last stage is reached, the patient may suffer but little in his general health. As time goes on, the sputum, which at first is mucoid, becomes muco-purulent; at times it is blood-streaked and in some cases frank hemoptysis occurs. In rare instances the sputum has a foul odor because of an associated bronchiectasis.

In the advanced stages of pneumoconiosis the pulmonary circulation becomes more or less distended by reason of the extensive fibrosis, and this may lead to embarrassment of the right heart. Constitutional symptoms are not marked. Fever is not a part of the picture, except in the terminal stages when secondary pulmonary infections may occur. When constitutional symptoms develop, a superimposed tuberculous infection is to be suspected.

Physical Signs.—In the examination of the chest of an individual exposed to inorganic dust, it is essential to know the length of time of the exposure and the type of dust. For instance, a coal miner or a potter who shows marked changes in the lungs and has followed either of these employments for a few years only, is not suffering from pneumoconiosis. Either of these occupations requires years to bring about changes demonstrable by physical examination. If changes are present, they are in all probability to be ascribed to other causes. Silicosis, on the other hand, may bring about demonstrable changes in the lungs in a relatively brief period.

The early changes are negligible and give no evidence of their presence. As the process advances to the second stage, which is readily demonstrated in the roentgen-ray films, abnormal physical signs are still absent or but very slight. When the disease becomes fully established, it will be noted on *inspection* that the expansion of the lungs is deficient, sometimes more marked on one side than the other. Retraction of one or the other side may be noted. If the fibrosis predominates in one lung, the heart may be drawn toward that side. The apex beat may be obscured by emphysema, which is often a prominent feature at the bases and along the free margins of the lungs. If the emphysema is at all extensive, the chest assumes the usual shape seen in that condition.

On *palpation* the lack of expansion is noted, and over densely fibroid areas the vocal fremitus may be exaggerated. In the early stages, the *percussion* note is not at all or but very slightly impaired. In the third or advanced stage, the note varies with the underlying condition. It may be impaired or decidedly dull in certain areas, notably the apices, the bases or interscapular regions. These areas may be bilateral or unilateral. If dilatation of the bronchi is present, a tympanitic quality may be present. This change is most apt to be noted at the apices or in the

interscapular regions. Along the free margin and often at the bases, the associated emphysema may give hyperresonance. Partly because of the inelasticity of the lungs and partly because of fixation of the diaphragm, the respiratory excursion of the lungs at the bases is very slight or even absent.

The signs on *auscultation* vary with the stage. In the beginning little or nothing abnormal may be heard. Even in the second stage, with numerous small areas of fibrosis scattered throughout the lungs, but little abnormal may be elicited. While the signs of bronchitis, namely, scattered rales, may be heard at any time, as a rule rales are heard only in the third or advanced stage. In addition, the breath sounds, because of the associated emphysema, become feeble and the expiration prolonged. If large areas of fibrosis form, fine crackling rales may be heard over these areas, and the voice sounds are exaggerated. The breath sounds may be harsh and broncho-vesicular in character. Friction rubs are frequently heard.

Inasmuch as bronchiectasis is common, cavity signs may be simulated. The common sites are at the apices or in the interscapular regions. In the latter situation, cavity signs usually mean dilatation of the bronchi; at the apices they may be due to dilated bronchi or to a tuberculous cavity. Clubbing of the fingers is not uncommonly seen because of the frequency of an associated bronchiectasis.

The heart shows no changes until the advanced stage, when embarrassment of the circulation may arise as the result of obstruction to the pulmonary circulation.

Roentgen-ray Examination.—The greatest advance in the recognition of pneumoconiosis is the use of the roentgen-rays. By this means it is now possible to trace the evolution of the process from the earliest manifestations to the final stage. In 1917, Lanza and Childs¹ presented the first American classification of the different stages based on roentgen-ray findings. Independently of these observers, Pancoast, in a study of pneumoconiosis, with Miller and myself,² adopted a similar classification. Briefly described, these stages are as follows:

1. Root shadows are denser and more extensive and may show nodules; the trunk shadows are increased in density and breadth, with numerous punctate deposits of varying size along them; the appearance is symmetrical on both sides at first, but not so later; there is no difference in the diaphragmatic excursion.

2. In addition to the foregoing, fairly symmetrical small, circumscribed, dense areas are found throughout both lungs, and later large masses accumulate, usually at the lower part of the upper third, about the level of the root shadows. The mottling in the beginning is more perceptible on the right side than the left, but later there is no appreciable difference. Owing to the small collected fibroid areas the hilum often presents the so-called "snow-flake" appearance. The domes of the diaphragm seem accentuated. In this stage the diaphragm begins to show limitation of motion, especially at the outer portion of the two leaflets.

¹ U. S. Public Health Bulletin No. 85, January, 1917.

² Am. Jour. Roentgenol., 1918, 5, 129.

3. This differs from the second only in the extent of the lung involvement, indicated by increased number of deposits and more massive grouping. In cases with massive fibrotic changes, the trachea, heart and great vessels may be displaced. In this stage the diaphragm is markedly restricted and often shows sharp peaks or other deformities.

Although other observers have somewhat modified or elaborated this classification, for practical purposes it remains the most satisfactory. A very comprehensive review of the subject has been made by Pancoast and Pendergrass.¹

It is to be borne in mind that the changes are not due to the dust itself (except possibly metallic dust) but to the fibrosis which the dust causes. In the first stage, the changes are almost entirely due to fibrosis or lymph block. As the process advances, the changes beyond the hilum limits become more marked. As the deposits of dust increase, the fibrosis increases. In some instances the small fibrotic areas appear as innumerable small shadows but more often they are less numerous and somewhat larger. In the late secondary stage or beginning third stage, the smaller nodules tend to coalesce, forming larger areas. In the third stage there is a diffuse fibrosis which, according to Pancoast and Pendergrass is of three different types: (1) The larger nodules where most prevalent may coalesce into much larger and irregular masses or be found together with more or less haze between. (2) A more frequent appearance is that of a more or less diffuse fibrosis with evidence of rather definite nodules still present. This form resembles closely the end-result of an extensive bilateral pulmonary tuberculosis. Pleural thickening is often present in both these forms. (3) The most striking change is a massive fibrosis in which a large area of the lung appears to be consolidated. As a rule, there is a large area of massive fibrosis in both lungs, but it may be limited to one side or it may be more extensive on one side. Associated with the areas of massive fibrosis are dense fibrosis bands extending in various directions, but usually downward and apparently connected with marked abnormalities of the diaphragm.

Roentgenologically it is not difficult to recognize the presence of pneumoconiosis, especially in the second and third stages. It is often difficult, however, to determine from the films alone whether there is an associated tuberculous infection. When the tuberculosis is still of the infiltrative type, it is not easy to distinguish it from the fibroid nodules which are due to deposits of dust. When the tuberculosis has advanced and cavity formation has taken place at the apex, it usually is recognized readily, and large fibroid areas are presumably tuberculous in character. In many cases the question of a coincident tuberculosis must rest on the presence or absence of tubercle bacilli in the sputum or resort to animal inoculation.

Complications.—Tuberculosis is the outstanding complication of pneumoconiosis. Pleurisy, emphysema, chronic bronchitis and fixation of the diaphragm are really a part of the general picture.

As a result of the massive fibrosis, one of the nerves passing through the thorax may become imbedded and interfered with. Pancoast and Pendergrass² report an instance in which one of the phrenic nerves was

¹ *Am. Jour. Roentgenol. and Radium Therap.*, 1925, **14**, 381.

² *Ibid.*

paralyzed, the probable explanation being that it was caught in a mass of fibrous tissue. I have under observation a patient with partial paralysis of the left recurrent laryngeal nerve, due in all probability to its having become involved in fibrous tissue, due to a chronic fibroid tuberculosis involving the left upper lobe.

Among the cobalt miners of the Schneeberg district in the Saxon Voigtland, primary sarcoma of the lung is said to be not infrequent. Irritation due to the inhalation of inorganic dust has been suggested as the predisposing factor. If this is true, the occurrence is unique, as among thousands of cases of pneumoconiosis examined, malignant disease of the lungs has not been found.

Diagnosis.—The recognition of pneumoconiosis is not difficult, except in those localities where it is rarely encountered and in this event a stray case nearly always causes confusion and errors in diagnosis. The essential features are: The occupation, the presence of dust, and the more or less characteristic roentgen-ray film. The physical examination may not reveal anything definite and respiratory symptoms may be absent or very slight. If, however, the individual has followed an occupation which subjects him to the dust hazard, and if in addition the roentgen-ray film shows pulmonary fibrosis, particularly if the fibrosis occupies the mid-portion and the bases of the lungs, the diagnosis of pneumoconiosis is almost certain. The only real difficulty is as to the presence or absence of tuberculosis. It is to be remembered that while pure, uncomplicated pneumoconiosis does occur, the condition is often complicated by tuberculosis. As a rule, the existence of an associated tuberculosis can be determined from the roentgen-ray films but this is not always possible. If the tuberculosis is of the chronic, ulcerative type with cavity formation at the apex, the diagnosis can be made with reasonable certainty from the roentgen-ray film. If, however, it is of the infiltrative type, it may be very difficult to distinguish between the tuberculous process and the pneumoconiosis. Large, massive fibroid areas may be due to the combined action of the dust and the tubercle bacillus, without the latter appearing in the sputum. As a rule, the presence of an associated tuberculosis is determined by the presence of bacilli in the sputum. Every case of pneumoconiosis should have repeated examinations of the sputum made. Another distinguishing feature is that pure pneumoconiosis rarely gives rise to constitutional symptoms, particularly fever. Such symptoms should of themselves suggest tuberculosis.

The most common error is made in the second stage of the disease when the roentgen-ray films show the lungs to be studded with small discrete nodules. These suggest miliary tuberculosis, and this diagnosis is usually made by the inexperienced.

Prognosis.—In the advanced stages with extensive fibroid changes in the lungs, dilatation of the bronchi and embarrassment of the heart, the outlook is bad and little can be done to alleviate the symptoms, particularly the dyspnoea. In the early stages the process may be arrested by removing the worker from exposure to the dust or seeing that preventive measures are installed in the working place. Removal from the hazard may do even more than arrest the process. It is now recognized that if

the worker is no longer subjected to the irritant dust, he may free himself from much that has already been deposited in the respiratory tract.

Treatment.—This is entirely preventive. Taken as a whole, the dust hazard is a problem for the public health officer and the sanitary engineer. In all occupations involving a dust hazard, every effort should be made to provide means for preventing its spread in the working place. Educational measures should be carried out among the workmen, as it is recognized that they are careless about availing themselves of safeguards, even when their advantages and the dangers of neglect have been explained to them.

Recognizing that individuals vary greatly in their susceptibility and that in a given period one man may show marked evidence of pneumoconiosis, while another shows little or nothing abnormal, it should be a rule that all men subjected to the hazard of dust inhalation be roentgen-rayed at least once a year. In this way the susceptible individuals can be detected. In the case of such individuals it would probably be wise to advise that they abandon that occupation.

CHAPTER VIII

DISEASES OF THE PLEURA

By FREDERICK T. LORD, M.D.

PLEURITIS

Occurrence.—From the point of view of the pathologist, pleuritis is very frequent. Including simple adhesions with other more marked changes in the pleura, pleuritis was found in 160 (74.4 per cent.) of 215 cases at autopsy (M. G. H.). Such processes pass undiagnosed in the great majority of patients, as is shown by the striking disparity between autopsy and clinical reports. Thus, of 35,207 patients admitted to the medical wards of the Massachusetts General Hospital, only 975 (2.7 per cent.) are recorded as suffering from pleuritis. Uncomplicated inflammation of the pleura is not a frequent cause of death.

General Etiology.—**Age.**—Pleuritis has been described in the newborn, but is relatively uncommon in infants. Pleuritic effusions in children are more often purulent and metapneumonic in origin, while in adults serous and tuberculous pleuritis is more common. Of 760 clinical cases (M. G. H.)¹ of different forms of pleuritis, about one-third of the cases occurred from twenty-one to thirty and more than one-half from twenty-one to forty.

Sex.—In general, males are much more frequently affected. In my series of 1681 patients with fibrinous, serofibrinous or purulent pleuritis, 1213 were males, 468 females.

Season.—A similar relation with the seasons obtains in pulmonary and pleural infection. Of 762 patients, of whom 248 (32.5 per cent.) sought the hospital clinic during March, April or May, the greatest number of cases for any month was 94 in March; while 189 (24.8 per cent.) presented themselves in June, July or August, 178 (23.3 per cent.) in December, January or February, and 147 (19.2 per cent.) in September, October or November.

Bacterial Etiology. It is impossible to separate the inflammations of the pleura into sharply-defined groups according to their bacterial etiology. The number of organisms concerned is comparatively small, and in the great majority of cases comprises the tubercle bacillus, the pneumococcus or the streptococcus. The limited number of different organisms concerned is probably due to the relation of the pleura to the deeper parts of the respiratory tract, where mixed infections are less common. The tendency of the tubercle bacillus to invade the sub-pleural tissue or the thoracic glands explains its frequent invasion of the pleura.

¹ Children comprise only a small number of the total admissions to the Mass. General Hospital.

Classification.—The terms “primary” and “secondary” are convenient for the description of clinical cases. Pleuritis is in reality only very rarely primary, almost always secondary to disease of neighboring organs, especially the lung. When cases are referred to as primary, therefore, it should be understood that the starting point of the disease in other organs has not been detected.

Acute Fibrinous Pleuritis; Fibrinous or Plastic Pleuritis.—The examination of cases with fibrinous pleuritis at the postmortem table shows that small amounts of fluid are usually present. From its clinical importance, however, the group deserves separate consideration.

Etiology.—The cases fall into two principal groups, those in which the disease is apparently (1) primary and those (2) secondary to disease of the lung or other part of the body.

1. *Primary.*—This forms the largest group in clinical cases. The disease seldom occurs in perfectly healthy individuals, and some disturbance of the respiratory tract may precede, but more often accompanies, the stitch in the side. In this series, 223 (64.6 per cent.) of 345 cases belong to this class. The clinical history and subsequent course of primary dry pleurisy indicate that it is due to tuberculosis in the vast majority of the cases.

2. *Secondary.*—The disease may be secondary to infective processes in any part of the body. Disease of the lung occupies first place and bronchitis is an important factor. It is probable that small areas of pulmonary invasion, too small to be detected on physical examination, frequently accompany bronchitis, and bacteria pass from the peripheral parts of the lung to the pleura. Pulmonary or bronchial gland tuberculous infection is the starting point of pleural infection in a large proportion of cases. In this series there was probable or certain pulmonary tuberculosis in 18 cases (5.2 per cent.), of which 6 showed tubercle bacilli in the sputum. Lobar pneumonia is represented by 15 cases. Bronchopneumonia, abscess, gangrene and bronchiectasis are less frequent causes. Of infections in more remote parts of the body may be mentioned acute or chronic endocarditis, tonsillitis, pyorrhœa alveolaris, arthritis, pericarditis, typhoid fever and uterine sepsis. Dry pleurisy is not infrequent in the later stages of all chronic diseases. Trauma with or without gross injury of the tissues may lead to fibrinous pleuritis and usually by infection from the lungs. Pulmonary infarction is an occasional cause. If the venous thrombosis is latent and hemoptysis does not occur the pleurisy may be regarded as primary.

Relation to Tuberculosis.—The proportion of cases in which the tubercle bacillus is responsible cannot be definitely stated. A study of my cases suggests that this form of pleuritis as an apparently primary affection is tuberculous in about the same proportion of cases as in primary serofibrinous pleuritis. This seems to be indicated by the subsequent course (see Prognosis, p. 226). It should be noted, however, that coincident tuberculosis was demonstrated in a smaller proportion of cases of fibrinous (5 per cent.) than of serofibrinous pleuritis (13 per cent.).

Pathology. The inflamed pleura lacks its normal lustre, is dull, opaque, coarsely or finely granular, grayish-white, or reddish, and deeper red in

places where ecchymoses are present. The membrane is thickened and may reach a centimeter or more in width. The surface of an abundant exudate may be thrown into folds or projecting masses of various shapes. There is practically always more than the normal amount of pleural fluid and this is usually cloudy. The extent of pleural involvement varies from a part to the whole of the pleura. It is not uncommon to find some extension of the inflammation along the interlobular septa in severe fibrinous pleuritis.

On microscopic examination, desquamation and degeneration or absence of epithelial cells are found. The subserous tissue is swollen and contains an increased number of polymorphonuclear cells. Lymph and bloodvessels are widened. The surface of the pleura is the site of a fibrinous layer containing numerous pus cells and serum. With the beginning of resolution the fibrin undergoes fatty metamorphosis and in mild cases may entirely disappear. In more severe inflammations the two layers of pleura become adherent. Organization, round-celled infiltration and connective-tissue formation take place, giving rise to adhesive pleuritis.

Site.—Of 323 cases in which the site of the process was noted, it was on the right in 134, on the left in 131, limited to the right upper chest in 20, to the left upper chest in 9. Of the remaining 29 cases, a situation at both bases in 7, in the diaphragmatic pleura in 3, and throughout the left side in 1 may be mentioned.

Symptoms.—Prodromata are relatively uncommon. Cough and expectoration, due to respiratory infection, may precede the stitch in the side. In a majority of the cases the onset is sudden, with pain, which varies much in intensity. An initial chill is rare. The temperature is often not elevated and was not above normal in 82 (23.7 per cent.) of 345 cases. A temperature of 99° to 100° or 101° F. is not uncommon. It may rise to 103° F. or higher, but high temperature is more often seen in complicated cases. The fever usually subsides within a few days.

Pain.—Pain is an almost constant feature. It may be absent after the acute symptoms have subsided or at the extremes of age. It is often described as sharp, stabbing or cutting, sometimes dull and dragging. It is usually circumscribed, rarely diffuse, and is felt in the axillary or mammary region, less commonly in the anterior or posterior lateral and lower parts of the affected chest. It may radiate to the shoulder or lumbar region, less commonly into the upper extremity, the neck or abdomen. The rare cases in which the pain is referred at first to the *abdomen* are troublesome for diagnosis. Of 145 cases this occurred in 8 (5.5 per cent.), and may have been due to diaphragmatic pleurisy. Pleuritic friction may be absent and the case may then present the picture of an acute abdominal affection. The pain is usually in the upper abdominal region. It may be accompanied by tenderness and muscular spasm and suggest an inflammatory abdominal condition. Laparotomy has been performed in cases in which a few days later the pleuritic origin of the symptoms became obvious. Capps¹ explored the pleural cavity by means of a wire passed through the cannula of an instrument for thora-

¹ *Trans. Assn. Am. Phys.*, 1910, 26, 486.

centesis. The visceral pleura seemed devoid of pain sense. Irritation of the parietal pleura gave rise to pain over the site of irritation. Irritation of the central portion of the diaphragmatic pleura caused pain in the neck, of maximum intensity along the ridge of the trapezius muscle (fourth spinal segment). Irritation of the peripheral rim of the diaphragmatic pleura elicited pain in the lower thorax, the lumbar region or the abdomen.

The pain of fibrinous pleuritis is usually of moderate intensity, at times almost unbearable, at others slight, and present only with a deep breath or cough. It may be continuous or intermittent, but is usually most marked at the beginning of the illness, disappearing suddenly or gradually within a week to ten days. In some cases it may last for weeks or months. Movement, laughter, pressure on or percussion of the affected side, quick change of position, even elevation of the arm, may start or aggravate it. With the advent of pleural effusion, pain diminishes or disappears.

Cough.—This is present in a large proportion of cases. Of 145 patients it was noted in 103 (71 per cent.). It was stated to be absent in 18, and the records are silent on this point in 24. It is usually ascribed to pleural irritation, and a relation with this is suggested by the frequency with which forced respiration excites cough and by its relief when the side is immobilized. It is probable that pulmonary infection plays a part in its production, for in 44 cases (30.3 per cent.) expectoration accompanied the cough and rales were noted in 45 (31 per cent.). The sputum lacks characteristic features. It was muco-purulent or purulent in many. In 6 cases it was bloody.

Dyspnœa.—Quick respiration may exist without dyspnœa. When it occurs, dyspnœa is usually slight. It may be due to fever, an effort to limit the excursion of the lung, because of pain, or to encroachment on pulmonary space by an effusion.

Physical Signs.—The position in bed is inconstant; at times some relief is afforded by lying on the affected and at other times on the unaffected side or with the upper part of the spine deflected toward the diseased pleura and the shoulder of that side depressed from the fixation and compression which this position affords. A diminished expansion of the involved side can be seen as well as felt, most often in the lower lateral thoracic region. The pulmonary excursion, as shown by percussion of the lower pulmonary margin at the end of inspiration and expiration and by the amplitude of the diaphragm phenomenon, is usually diminished for both lungs, much diminished or absent on the affected side, and the interspaces are slightly narrower. Percussion may be painful. No change in the percussion note can ordinarily be determined. The respiratory murmur is diminished and vesicular in character; the vocal fremitus may be diminished, but is usually unchanged.

Pleuritic Friction.—A friction rub can be heard and not infrequently felt as early as twelve to twenty-four hours after the onset. Its occurrence and resemblance to the creaking of leather did not escape Hippocrates. It is often jerky and may be inconstant, present during one, absent at the next respiration—such irregularity being due to alternate fixation and motion of the visceral against the parietal pleura. It may disappear

during the examination. The rub is more distinct during inspiration than expiration. Fibrinous pleuritis may exist without friction sound, and friction does not exclude fluid in a neighboring part of the pleura.

Pseudopleuritic Friction.—Students frequently confuse with pleural friction a sound often heard over the back in normal individuals. This is commonly heard during the examination of the posterior thoracic region while the patient's arms are folded across the chest, each hand resting on the opposite shoulder. It begins as an inconstant, rumbling, grating sound, at first confined to inspiration, becoming more and more intense and finally occupying both phases of respiration. It may be harsh and hardly to be distinguished by quality alone from pleuritic friction. It may be reproduced after an interval of quiet and heard in subsequent examinations. It is usually bilateral. At times it can be felt with the hand and may be audible several inches from the side. The patient may appreciate it as a grating sensation but it causes no pain. In the back it is confined to the scapular region and may be followed upward to a point of maximum intensity over the shoulder-joint. At times it can be heard along the clavicle and down the arms as far as the hand. Removal of the hands from the shoulders may abolish it. The sound is due to crepitus at the shoulder-joint. It is rougher than the sound heard over any contracting muscle of the extremities and is not a muscle sound. Its less jerky character, bilateral position over the scapulae, maximum intensity over the shoulder-joint, disappearance on shifting the arms and the absence of pain serve to distinguish it from pleuritic friction.

Pleuro-pericardial Friction.—This is not infrequent and is often difficult of interpretation. It may be due to inflammation of the pulmonary, costal, or that part of the mediastinal pleura overlying the heart. It is likely to be influenced by the movement of the heart as well as by respiration. Owing to the variable line of reflection of the left costal pleura over the cardiac region, a distinction between pericardial and extra-pericardial friction cannot always be safely made from its situation alone, but in general it may be said that pleuro-pericardial friction is uncommon over the superficial cardiac dulness, and is usually heard outside this region. It is influenced more than pericardial friction by the respiratory movements. If the patient stops breathing, the friction sound may diminish or disappear.

Pseudopleural Intrapulmonary Sounds.—Loud sonorous rales may occasionally simulate pleural friction. Their less jerky character and disappearance after cough may suggest their pulmonary origin.

Pleural Crepitation.—At times with symptoms of pleuritis, fine, inspiratory crepitations are heard over the site of the suspected process. This may be pleural in origin, but can hardly be differentiated from intrapulmonary rales.

Roentgen-ray Examination.—There is usually no direct evidence on radioscopic examination of the presence of an acute fibrinous pleuritis as the thin layer of inflamed pleura is permeable to the rays. Such indirect evidence as a general haziness, from incomplete expansion, narrowing of the intercostal spaces, and elevation and immobility of the diaphragm on the affected side may be obtained. Abnormal appearances

in the lung fields may suggest the cause of the dry pleurisy. In the apparently primary form the roentgen-ray findings may suggest pulmonary tuberculosis.

Blood.—*White Cells.*—Fibrinous pleuritis is more often accompanied by leukocytosis than serofibrinous pleuritis. Thus, of 48 cases of primary fibrinous pleuritis, the white count was 12,000 or over in 19 (39.5 per cent.).

Sequelæ.—Of 345 cases, pleural fluid was discovered as a sequence of the process in 5.

Diagnosis.—This is usually easily made from the presence of a friction rub. Cases with acute onset, with cough and stitch in the side, aggravated by respiration, are due to pleuritis in a large proportion of the cases, even if no friction rub can be heard. The diagnosis of diaphragmatic pleurisy is often troublesome and may remain in doubt for several days. Cases in which pain along the lower thoracic margin is the only symptom are most difficult of diagnosis. To judge from the remarkable frequency with which there is postmortem indication of previous disease of the pleura, it is probable that an undetected pleurisy is the cause in a large proportion of the cases. Rarely the pain is the precursor of herpes zoster. Pulmonary embolism and infarction is a possible cause of an apparently primary dry pleurisy. Phlebitis is not always manifest and the embolus may come from a pelvic, abdominal or thoracic vein. The possibility of spinal disease must be borne in mind. Tertiary syphilis and tumor are to be considered. Lead poisoning, caries of the ribs, periostitis and thoracic aneurism should be excluded. The roentgen-rays help in the diagnosis. A diagnosis of pleurodynia or intercostal neuralgia amounts to a confession of ignorance concerning the cause of the process.

In typical cases there is little danger of confusion, but the signs may be those of thickened pleura, dullness, diminished vesicular breathing, with preservation of the fremitus, even a friction rub, and yet fluid may be present. The fluid may exist between lung and diaphragm, where small amounts are likely to collect first, and rise little above the pulmonary margin between lung and chest wall. In other cases there may be evidence of thickened pleura and oftenest in the lower anterior aspect of the chest, with fluid in the posterior, inferior thoracic region. Again, fluid may be encapsulated and fibrinous pleuritis with friction coexist. In doubtful cases an exploratory puncture must be made. Cases with complicating pulmonary disease are likely to cause most difficulty in diagnosis.

Primary dry pleurisy should be regarded as probably tuberculous in origin. Preceding good health, satisfactory general condition and mild symptoms are not to be regarded as sufficient evidence against this diagnosis. Primary dry pleurisy, as an indication of tuberculosis, is equal in significance to primary pleurisy with serofibrinous effusion or hemoptysis out of a clear sky.

Prognosis.—The immediate outlook is good. The more remote prospects are less favorable. Of 82 cases of primary dry pleurisy¹ 60 have been followed since their discharge from the hospital. Of these, 18 (30 per cent.) certainly or probably developed tuberculosis. Their subsequent

¹ Lord: *Boston Med. and Surg. Jour.*, 1909, 160, 469.

course has been followed from one to twelve years, the average interval being four or five years. The outcome of primary dry pleuritis is thus nearly or quite as bad as that of primary serofibrinous effusion. The prognosis of the secondary form is that of the underlying cause. Pain may persist after the attack; 15 patients (25 per cent.) complain of occasional or persistent pain.

Treatment.—The immediate indication is the relief of pain, on which the dyspnoea largely depends. *Rest* is the first consideration. In all cases in which there is fever or severe pain, the patient should be in bed. Even in mild attacks, rest shortens the duration and may prevent extension or the occurrence of an effusion.

Fixation of the side limits the play of the pulmonary against the parietal pleura and may produce immediate relief. It may be accomplished with adhesive plaster, of which zinc oxide plaster is best. The plaster should not be allowed to remain longer than a week to ten days, and care taken in its removal not to cause abrasion of the skin. A tight thoracic swathe, with shoulder and peroneal straps, has the advantage of ready removal for physical examination, and does not lead to irritation or infection of the skin. It is to be preferred for patients in bed. In some cases, perhaps from diaphragmatic involvement, fixation of the thorax fails to give relief. In such cases an ice-bag or hot-water bottle may be efficient. If these means fail, a hypodermic of morphine may be given.

A possible source of infection should be sought, and if found in any part of the body, should receive appropriate treatment. A dry pleuritis should always suggest the possibility of tuberculosis. All cases of *primary* fibrinous pleurisy, even the mildest forms, in patients otherwise in apparent health, should be treated as if tuberculous until the pleuritis can be proved to be due to another cause. The physician's responsibilities do not end with the apparently favorable outcome of the acute attack. No matter how mild this has been or how reassuring the general condition appears to be, permanent results can be attained only by supervision at regular intervals and instruction to report at once on the occurrence of another attack, failing health, rise of temperature or other suspicious symptoms.

Acute Serofibrinous Pleuritis.—**Etiology.**—Serofibrinous effusions arising from inflammation of the pleural sac may be divided into three principal groups: (1) *Tuberculous pleuritis* comprises the largest and most important division. (2) *Infectious (non-tuberculous) pleuritis* stands next in frequency and is a well-defined class. (3) *Other causes* are relatively infrequent and often difficult to group. They are the product of more than one factor, such as general hydremia or venous stasis, on which an inflammatory process is superimposed.

1. **TUBERCULOUS PLEURITIS.**—It is remarkable in how many cases serofibrinous pleuritis is apparently primary without evidence of disease in other organs. Thus of 1185 cases the disease of the pleura was unassociated with positive findings elsewhere in 750 (63.4 per cent.). The pleural disease was combined with suggestive or positive evidence of tuberculosis elsewhere in 160 (13.5 per cent.). The lung was the most frequent site of tuberculosis with 149 cases, of which 47 showed tubercle bacilli in the

sputum. Tuberculous peritonitis was present in 9 and tuberculosis in other regions in 2 patients.

There is good reason to believe that a large proportion of cases of serofibrinous effusion, more especially the primary cases and those secondary to pulmonary tuberculous lesions, are due to tuberculosis. This point of view is based on the following:

(a) *Tuberculosis of Other Organs.*—In Osler's 195 cases, 30 showed tubercle bacilli in the sputum. Pleural effusion as a symptom of pulmonary tuberculosis usually comes early if at all. Dense pleural adhesions commonly obliterate part or the whole of the pleural sac in an advanced stage of the disease.

(b) *The Subsequent History.*—The after histories of 130 cases of primary pleurisy with effusion by Hedges¹ showed that at least 40 per cent. died of or had tuberculosis within six years. Osler² refers to 86 cases of which 34.8 per cent. became tuberculous and died. The subsequent course of 90 cases of primary pleurisy, irrespective of type, was investigated by V. Y. Bowditch,³ and 32 (35 per cent.) died of or had phthisis. Sears⁴ found that of 86 known to have died the cause was some form of tuberculosis in over 55 per cent.

(c) *Postmortem Evidence.*—Of 131 cases of different types of pleuritis examined postmortem by Osler, 32 were found tuberculous.

(d) *The Tuberculin Reaction.*—This is positive in a large proportion of the cases—in 73.7 per cent. of Beck's series and in 7 of 8 cases by F. W. White. In my series (M. G. H.) tuberculin was given in 47; 36 (76.5 per cent.) gave a positive reaction. A positive result merely means tuberculosis somewhere, not necessarily in the pleura.

(e) *The Character of the Exudate.*—The evidence is based on the character of the cells, the demonstration of tubercle bacilli in the fluid, and the results of animal inoculation. *Lymphocytes* predominate in a large proportion of serofibrinous fluids from patients known to have tuberculosis of the pleura. Excess of lymphocytes is not invariably proof of a tuberculous pleurisy.

(f) *Tubercle Bacillus in the Fluid.*—The effort to cultivate tubercle bacilli from serous effusions practically always fails. Simple microscopic examination likewise is usually unsuccessful. In 115 cases at the Massachusetts General Hospital in which tubercle bacilli were sought in the fluid, they were found in 24 (20.8 per cent.). Kőrmöczy and Jassniger⁵ found bacilli in 3 of 8 cases. Zebrowski,⁶ by simple sedimentation of a large quantity of fluid, prevented from coagulation by the addition of sodium fluoride, found bacilli in 12 (55 per cent.) of 22 primary cases and in 10 (83 per cent.) of 12 secondary effusions.

(g) *Animal Inoculation.*—The most convincing evidence is obtained by animal inoculation. Of 66 cases in my series the results were positive in 15 (22.7 per cent.). Le Damaney,⁷ by the inoculation of 10 to 50 and at

¹ *St. Bartholomew's Hosp. Rep.*, 1900, **36**, 83.

² *Brit. Med. Jour.*, 1904, ii, 999.

³ *Trans. Am. Climat. Assn.*, 1889, **6**, 1.

⁴ *Boston Med. and Surg. Jour.*, 1904, **150**, 209.

⁵ *Deutsch. med. Wchnschr.*, 1904, p. 342.

⁶ *Ibid.*, 1905, No. 36.

⁷ *Presse méd.*, November 24, 1897. p. 329.

times as much as 300 cc., obtained positive results in all but 8 (8.5 per cent.) of 55 primary cases, while in 4 of the 8 negative cases coincident lesions indicated their tuberculous origin. By the presence of tubercle bacilli in the sputum, in the fluid by animal inoculation or inoscopy, or by operation, Musgrave proved the tuberculous character of 28 (54.9 per cent.) of 51 primary or secondary effusions.

2. **INFECTIOUS (NON-TUBERCULOUS) PLEURITIS.**—Infection of the pleura with other organisms than the tubercle bacillus is capable of causing serofibrinous effusion. The pneumococcus is the most frequent cause in this group. The streptococcus and other organisms may likewise be a cause. A difficulty lies in the exclusion of the tubercle bacillus as a mixed infection.

(a) *Metapneumonic Pleuritis.*—This is a well-defined group and is represented by 62 (5.2 per cent.) of 1185 cases with serofibrinous effusion. Small effusions of a serofibrinous or purulent character are common in lobar pneumonia. Maragliano demonstrated serofibrinous or purulent effusion in 38 of 58 cases, by exploratory puncture. If small amounts are included, a serofibrinous is more common than a purulent exudate. Of 154 autopsies on cases with lobar pneumonia (M. G. II.), a pleural effusion was present in 55. The fluid was cloudy in 30, clear in 10, purulent in 9, and hemorrhagic in 6. The largest amount at autopsy was 500 cc.

(b) *Rheumatism.*—This was coincident with pleuritis with effusion in 13 cases (0.9 per cent.). There is no proof that the rheumatic infection can infect the pleura alone and give rise to pleurisy of a primary type. It is possible however that such cases occur and the matter must remain in doubt until the cause of rheumatic fever is established. Pleuritis occasionally occurs in rheumatic fever, and I have seen 8 cases. There was coincident arthritis in all. Constant involvement of the left side and the right also in one suggests that the pleuritis arises as an extension from pericarditis, which was demonstrable in 6 and doubtful in 2. Fluid was obtained for examination in 4. It was slightly cloudy, yellowish, with a specific gravity of 1015 to 1022 and with 1.6 to 3.6 per cent. of albumin. In the presence of rheumatic arthritis, pericarditis with effusion and sterile serofibrinous pleurisy the likelihood that the fluid in the pericardium is of the same character as that in the pleura may be used as an argument for the avoidance of tapping the pericardium unless other indications make such a procedure desirable.

(c) *Trauma.*—Serofibrinous effusion followed trauma in 10 cases (0.8 per cent.) in this series. The effusion may be due to simple infection or to tuberculosis.

(d) *Typhoid Fever.*—The association of serofibrinous effusion and typhoid is rare, occurring in only 7 cases (0.5 per cent.) in this series. Among 1500 cases of typhoid, McCrae¹ noted only 3 with serous effusion. The bacilli have been obtained in pure culture from the fluid. Pleural effusions in typhoid fever may also be hemorrhagic, but are most commonly purulent. The complication may occur early, but is more often found during the course. It is not certain that the typhoid bacillus alone

¹ Osler and McCrae's *Modern Medicine*, 1925, **1**, 115.

is capable of causing serofibrinous effusion. General infection with typhoid bacilli is so common in typhoid fever that the mere presence of typhoid bacilli in the exudate does not suffice to establish the independence of typhoid pleuritis. The agency of other organisms, and especially the tubercle bacillus, must be rigorously excluded.

(e) *Infection in any part of the body* may be a cause of serofibrinous pleuritis, although the effusion accompanying septic processes is more often purulent in character or becomes so after passing through a serofibrinous stage. Pulmonary infection resulting in bronchopneumonia, pulmonary infarction, pericarditis, malignant endocarditis, uterine sepsis, etc., may lead to serofibrinous pleuritis. In such cases the serous rather than the purulent character of the effusion may be due to the small number or diminished virulence of the infecting organisms or to increased resistance on the part of the patient.

3. **OTHER CAUSES**—A sharp, dividing line cannot always be drawn between transudates and exudates. An inflammatory process may readily be superadded to a transudate and thus complicate the differentiation.

Pathology.—1. *Pleura.*—The appearance of the pleura does not usually differ from that in simple fibrinous pleuritis. The fluid commonly occupies the most inferior parts of the cavity, and in acute cases the fibrinous layers on the two pleuræ are usually easily separated where they lie together above the fluid. Bands of adhesions may traverse the fluid and connect the visceral and parietal layers. In the more chronic cases the two pleuræ may be more or less firmly united above the fluid. It is less common to observe encapsulation of serofibrinous than of purulent fluid. Sacculated exudates are most common at the posterior and inferior aspect of the pleural sac. Rarely more than one encapsulation occurs, and the contents of the two may vary, in one serous, in the other purulent fluid. Miliary tubercles may occur in the pleura without fluid or fibrinous exudate. In its gross appearance the pleura may not differ from that in the simple form, and tubercles may be discovered only microscopically.

2. *Side Affected.*—The left side is the more frequent site of the process. Of 1085 clinical cases the effusion was confined to the left side in 570, to the right in 487, while both were involved in 28. In 1 the effusion was sacculated on the left, posteriorly, near the spinal column, over an area 8 inches in diameter.

3. *The Effusion.*—This is quite variable in its character. It may be largely serous, with only a small amount of scattered fibrinous flocculi. The fibrin may exist as wavy, skein-like masses in suspension, or as more compact, whitish, coarse, membranous shreds or curd-like deposits. A clot usually forms in a variable but short period after evacuation, and may be found as a small, jelly-like mass at the bottom, or may comprise almost the whole volume of the fluid, with only a thin layer of clear serum about it. The fluid is usually amber colored, with an admixture of greenish or reddish from the presence of blood. It may be brownish on removal or turn so after standing. When mixed with considerable blood it may be blood-red, and, if removed after having long remained in the chest, may be darker, even chocolate colored. With jaundice the fluid is more deeply colored and responds to the tests for biliary substances.

Most fluids are clear or only slightly opalescent from the presence of albumin in fine subdivision, fibrin in the form of flocculi, clot, fat or cellular elements. No sharp dividing line can be drawn between sero-fibrinous fluids cloudy from the presence of numerous cells and those with more or less frank admixture of pus. Cellular elements tend to sediment within as well as outside the chest, and an abundance of polymorphonuclear cells obtained on tapping the upper layers of a pleural fluid may be associated with a sediment of pus at the bottom.

(a) The *amount* of fluid is very variable. In acute fibrinous pleuritis there is practically always more than the normal amount of fluid in the pleural sac. Even when the process is confined to the upper parts of the pleura, small amounts are often found at the bases. In 500 cases the amount varied from a few to 4620 cc., the largest measured amount at one tapping. The right chest is more capacious than the left and larger amounts are usually present in men than in women.

(b) *Specific Gravity*.—The determination of this is of great value in differentiating exudates from transudates. Inflammatory fluids have a specific gravity of 1018 or over and of 224 cases only 19 had a specific gravity below 1018. The amount of salts and extractives is very nearly the same in fluids of different origin and after the removal of albumin, amount to about 1.08 per cent. in non-inflammatory fluids and to about 1.18 per cent. in inflammatory fluids. A variation in the specific gravity of pleural fluids is dependent for the most part on differences in the amount of albumin.

(d) *Albumin*.—This exists as serum albumin, serum globulin and fibrinogen, to which, if present in sufficient amount, is due the property of spontaneous coagulation. Inflammatory fluids contain a relatively large amount of albumin and fibrinogen. In general, exudates have 4 per cent. or more of albumin.

(e) *Fat, uric acid, cholesterol, glucose, biliary acids and pigments* are occasionally found. In Schulman's case,¹ 5 ounces of thick yellow fluid, containing 9.73 per cent. cholesterol, were obtained from the chest of a patient who had had an unevacuated effusion forty years previously. In Ruppert's² and Weems cases³ there was 1.29 and 1.39 per cent. respectively.

(f) *Cellular Elements*.—The sediment shows red blood corpuscles, polymorphonuclear leukocytes, small mononuclear (lymphocytes) and endothelial cells. Eosinophiles and mononuclear cells intermediate between the small lymphocyte and endothelial cell are common, but usually comprise only a small proportion of the total number. An occasional mast cell is not an infrequent finding. The cystology is further considered on p. 249.

4. *Intrapleural Tension*.—With small effusions this may still be negative. As the fluid increases the tension rises and becomes positive after the pulmonary elasticity is spent. Various factors influence the pressure. It may be relatively high with a small amount of fluid if pulmonary retraction is prevented by pleural adhesions, by pulmonary or mediastinal

¹ *Jour. Am. Med. Assn.*, 1917, **68**, 1256.

² *Munchen. med. Wchnschr.*, 1908, **60**, 510.

³ *Am. Jour. Med. Sci.*, 1918, **156**, 20.

disease. Pitres¹ finds that the pressure may vary from 0 to + 2 or + 3 with less than 1000 cc. from + 8 to + 22 with 1000 to 2000 cc., and from + 20 to + 48 mm. Hg. with more than 2000 cc. The pressure fluctuates with the phases of respiration. An initial positive pressure may fall during deep inspiration to -40, as noted by Schreiber.² After aspiration the fall may be greater and with deep inspiration even to -90 mm. Hg. The fluid is also under a pressure of its own fluid column and the tension thus varies at different levels.

5 *Mechanical Effects of the Exudate*.—With small effusions the lung contracts and becomes atelectatic. With large effusions it is compressed, completely emptied of air, and for the most part of blood, and may be found as a brown mass, not larger than the closed fist, lying against the spinal column in the upper and posterior part of the affected side. In the absence of long-standing and extensive inflammatory changes it is still capable of reëxpansion after removal of the fluid. Under less favorable circumstances, extensive adhesions, the formation of dense connective tissue on its surface and within its substance may prevent this. Such a result is much less common with serofibrinous than with purulent exudates, and since it has become the custom to tap early.

In consequence of diminished negative pressure within the thorax, the intercostal spaces show less than their normal depression. Early in the disease they may be narrowed from spasm of the intercostal muscles. With a large effusion and increase in size of the affected side the spaces may actually be widened from pressure, and perhaps, also from paralysis of the intercostals. Later, following the absorption or removal of fluid, the thoracic wall may be depressed, and the intercostal spaces narrowed from contraction of scar tissue. The diaphragm, and with it the liver or spleen, is at first depressed from the loss of the normal negative intrathoracic pressure. With large effusions, the diaphragm is forced downward by positive pressure from above and the weight of the superimposed fluid. The dislocation of the mediastinum and the heart from small effusions is a result of a disturbance of equilibrium between the two pleural sacs. It is dislocated by positive pressure with large effusions. Pressure on the œsophagus may lead to dysphagia, and pressure on or invasion of the region about the vagus to recurrent laryngeal paralysis.

6. *Absorption*.—Various factors probably play a part in absorption. Hydræmic and congestive transudates are rapidly absorbed under favorable conditions. Inflammatory fluids containing relatively few formed elements and fibrin may likewise spontaneously disappear. Purulent fluids, however, may remain indefinitely unless evacuated by perforation or operation. Large effusions are less often absorbed. The mechanism is probably largely mechanical. Small, serous effusions, unassociated with fibrinous obstruction of pleural lymphatics, and interfering relatively little with respiratory changes of intrapleural pressure, are most favorable for absorption, while the opposite obtains in large and inflammatory fluids.

Symptoms.—1. PRIMARY FORM.—Prodromata are uncommon. Slight cough and failing health may precede the onset. An initial chill is rare;

¹ *Arch. clin. de Bordeaux*, 1896, 5, 70.

² *Deutsch. Arch. f. klin. Med.*, vol. 33.

chilliness is common. The disease began gradually in more than one-half (60 per cent.) of my series. There is malaise, pain of variable intensity, fever and cough. A sudden onset, in which the patient's activity is abruptly interrupted, is less common. In exceptional cases the initial features suggest pneumonia. There is chill, fever, and severe pain in the side, but no rusty sputum. An insidious onset, especially at the extremes of age, is not infrequent. In a small proportion the symptoms are sufficiently characteristic to suggest the diagnosis from the history of initial pain, which gradually diminishes or stops as the fluid accumulates and the dyspnoea increases. The temperature may rise gradually as long as the fluid increase is continuous during this period, intermittent with the effusion at a standstill, and often absent during absorption. It may reach normal at the end of a week or ten days, although continuous or irregular fever may last for a much longer period. The exudate may be discovered by the third or fourth day; if untapped may gradually increase during the next ten days, then gradually diminish, to disappear in favorable cases during the third, fourth, or fifth week.

The disease is often atypical. General symptoms and fever may predominate, and, aside from the pulmonary findings, typhoid fever may be suggested. Pain in the abdomen, with muscular spasm and tenderness, may suggest an acute abdominal affection. Both onset and course may be latent or sudden, severe, even rapidly fatal (*pleuritis acutissima*). There may be an initial chill, rapid rise of temperature, intense dyspnoea, cyanosis, rapid pulse and respiration, delirium and death in a few days with symptoms of suffocation. An immediate resort to evacuation may be life-saving in such cases.

2. SECONDARY FORM.—The onset and course are often so masked by the existing disease that symptoms referable to the pleura are unnoticed or absent. Pleural effusion may then be discovered only during a routine physical examination, or, if this is neglected and the disease is fatal, at autopsy. The presence or absence of symptoms largely depends on the mildness or severity of the primary disease. In pulmonary tuberculosis, however, the symptoms may be typical, since effusion usually occurs early, if at all, in its course, from the frequent obliteration of the pleural sac by adhesions in the more advanced stages. In lobar pneumonia, typical symptoms of effusion are usually lacking or only with difficulty differentiated from those due to the pneumonia itself. There may be an accession of pain, dyspnoea or cough. The respirations, pulse, and temperature may rise above their previous level. A failure of the temperature to drop at the expected time may be the first indication.

3. SPECIAL SYMPTOMS.—*Pain*.—This is usually one of the first and most typical symptoms. It was present in 89 of 100 cases of primary serofibrinous effusion in this series. It may be absent, as in 5 cases. Associated tenderness over the inflamed pleura is frequent.

Cough.—This is probably next in frequency, occurring in 83 per cent., absent in 12 per cent. and not given in 5 per cent. It is usually short and dry, but may be accompanied by expectoration (48 per cent.). The sputum is mucoid or muco-purulent; rarely it may contain blood (2 per cent.). Cough alone may be due to pleural irritation. Expectoration

should suggest a pulmonary complication, usually an infection, more rarely œdema, evidence of which may be furnished by the character of the sputum.

Respiration.—Short, quick respiration is frequent in the early stages from pain and spasm of the respiratory muscles. The rate may be elevated from fever, encroachment on the thoracic space by fluid, associated pulmonary disease, or embarrassment of the circulation from pressure. The normal relation between the rate of respiration and pulse is much more often maintained with pleural effusion than with pneumonia. Quick respiration is more often observed at the onset and after exertion. When the patient is at rest and the exudate has gradually accumulated, one side of the chest may be filled with fluid without disturbance of the normal respiration-pulse ratio.

Dyspnœa.—The embarrassment of respiration may amount to dyspnœa. This is more frequent in rapidly formed and large accumulations, and may become orthopnœa. At times, with small effusions and much limitation of respiratory motion, there may be marked dyspnœa. Cyanosis, with or without turgescence of the cervical veins, is likely to accompany marked interference with respiration.

Temperature.—There is no typical fever curve. The temperature is more often elevated and in general reaches a higher level than with dry pleurisy. Of 100 primary cases only 10 were without fever. From 100° to 102° F. is an average pyrexia. In rare instances the temperature may reach 104° to 105° F. or higher. It is likely to be high in children and robust patients. Absence of fever is occasionally observed in old or debilitated patients and in terminal infections.

Pulse.—This presents no special features. The rate usually corresponds to the fever. The rapid accumulation of a large amount of fluid may embarrass the circulation and cause a rapid and feeble pulse.

Febrile or Toxic Symptoms.—These are such as may be seen in other infectious processes. At the onset there may be headache, insomnia, malaise and general pains. The skin is hot and dry. As the fever drops, sweating may become a prominent feature. There may be thirst, anorexia, even nausea and vomiting, but gastric disturbances are uncommon. In protracted cases the loss of strength and weight may be marked.

Hoarseness may be due to pressure on or paralysis of the recurrent laryngeal nerve. *Dysphagia* from pressure on the œsophagus may be present. Ferber observed that the passage of food through the œsophageal foramen may be accompanied by pain, when there is diaphragmatic pleurisy. *Singultus* is rare but may be most distressing when the diaphragm is involved.

Urine.—During the acute stage, the urine is small in amount, of high color and specific gravity, with increase of urea and uric acid and diminution in chlorides. During absorption, the amount may rise rapidly with increase in chlorides, the so-called "chlorine crisis," while urea and uric acid are diminished. Traces of albumin and a few hyaline casts may be present and can be ascribed to fever, toxemia, or rarely to stasis.

Physical Signs.—Small amounts of fluid collect in the most dependent part of the thoracic cavity, in the costo-phrenic sinus posteriorly, and

between the lung and diaphragm. Until the amount becomes considerable, it intervenes very little between lung and chest wall. In Garland's experiments there was scarcely a trace of a rim of fluid between the lower border of the lung and the chest wall, with injections which occupied less than one-third of the thoracic cavity. In explanation it is assumed that there is a greater elastic traction in the lower than in the upper parts of the lung. Larger amounts finally intervene between lung and chest wall. In favorable and uncomplicated cases, 250 cc. of fluid in an adult should not escape detection. In infants 100 cc. may be discovered.

Inspection.—Herpes is uncommon. Inspiratory dilatation of the alae nasi is less frequent than with pneumonia. The position is variable. If there is dyspnoea, the patient may be more comfortable sitting upright, from the greater mechanical advantage and from the removal of the weight of the effusion on the lung which this position affords. With small effusions, without orthopnoea, the patient may be more comfortable on the unaffected side. The explanation of this is not clear. It may be due to the relief of pain from removal of pressure on sensitive nerves in the affected pleura. With large effusions, the patient usually chooses a position on the affected side, thus allowing the sound lung full play and diminishing pressure on the mediastinum. It is not uncommon, even with large effusions, to find the patient lying comfortably on the back. At times an ambulant patient presents himself with a large effusion.

In the early stages when there is pain and only a small amount of fluid, the appearance of the thorax does not differ from that described under fibrinous pleuritis. With increase in the amount of pleural fluid, there is progressively less expansion and elevation of the affected side. The presence of pain always still further limits thoracic motion. Diminished motion may often be apparent as a delay in expansion of the lower parts of the chest during the first part of inspiration. With large amounts of fluid, expansion and elevation may be absent. The intercostal spaces in spare individuals may be seen to have lost their normal depression and may even be widened and fuller than normal. An increase in size can be confirmed by the tape, even as much as 1 inch or $1\frac{1}{2}$ inches greater than the opposite side. The skin may appear somewhat shiny and smooth from obliteration of normal furrows and depressions. Œdema of the skin and dilatation of the superficial veins may occur, but are rare with serous effusion.

In consequence of fulness of the affected side, the distance between the median line and the nipple in front and the scapula behind may exceed that on the normal side. With large effusions the corresponding hypochondrium may be fuller. The shoulder and with it the outer end of the clavicle stand at a higher level. Following partial or complete absorption or withdrawal of fluid, the affected side may be somewhat diminished in size and the intercostal spaces narrowed. Slight lateral deviation of the spine may accompany this retraction. Retraction and scoliosis are much less marked after serous than after purulent fluids.

The *diaphragm shadow* is absent on the side of the effusion. It usually remains absent after recovery, but may return, although practically always of diminished amplitude. The position of the cardiac impulse

should be noted. Evidence of pleuro-pericardial adhesions may be obtained by systolic depression of the intercostal spaces in an abnormal position in the cardiac region.

Rarely *pulsation* of the chest wall may be observed with serofibrinous effusion, but is more common with pus. The pulsation may be confined to a locally bulging area; it may be circumscribed without tumor or may be diffuse.

Palpation.—This may confirm inspection. A difference in expansion of the two sides of the chest, the condition of the intercostal spaces, degree of separation of the ribs, position of the cardiac impulse and pulsations in other parts of the chest may be more evident to the hand than the eye. A narrowing and more marked resistance to pressure in the interspaces may occur early in the disease from spasm of the intercostals. The interspaces may be narrowed even when the affected side is increased in size. A friction rub may be felt before the onset of effusion; it may be palpated outside the limits of fluid during the course of the disease and may return following absorption. The temperature of the affected side is higher. Œdema and fluctuation are rare with serous effusion. The liver or spleen may be displaced downward. The diaphragm may be so far depressed as to be felt below the costal margin.

The *tactile fremitus* is practically always absent; it is rarely present, but usually even then diminished, in children, with adhesions between the visceral and parietal pleura or with small effusions. This is one of the most important signs of fluid. The dividing line between lung and fluid can often be sharply drawn at the level at which the voice vibrations are lost. The tactile fremitus above the fluid may be diminished, maintained, or increased, depending on the condition of the pleura and the lung. Unfortunately, fremitus cannot always be obtained in women or children, owing to the high pitch of the voice or the presence of abundant subcutaneous fat. Acute or chronic inflammatory thickening of the pleura diminishes, although it practically never abolishes, the fremitus. In thoracentesis, a localized area where fremitus is maintained should not be chosen, because of the possibility of pleural adhesions at this place.

Percussion.—Light is far superior to heavy percussion in bringing out slight changes in the pleura. Early in the disease, when there is only a small amount of fluid, no change in the percussion note may be detected. As the fluid increases there is dullness at the base. As the fluid rises, the note becomes less resonant and finally flat. The regions of flatness and absent tactile fremitus correspond. The percussion note over effusions of considerable size is of short duration, lacking in volume, of high pitch, very nearly like the note obtained on percussing the thigh. It is very difficult to mark on the chest the exact upper limit of fluid. With considerable fluid, three zones with well-marked differences in the percussion note can be made out in the anterior and more often in the posterior thoracic regions. Normal or diminished resonance may be obtained in the uppermost parts of the chest. Between this region and the fluid the note is dull, but has a tympanitic quality (Skoda's resonance), due to retraction or compression of the lung and vibration of air in the bronchi or trachea. Below, there is flatness from fluid. The intermediate

dull or dull and tympanitic area is usually most marked behind, in the interscapular region, but with large effusions may be detected in front, under the clavicle. If an arbitrary distinction be made between resonance and dulness and dulness and flatness, a triangular area of dulness or dull tympany can be marked out in the interscapular region, between the relatively normal lung above and the fluid below. This triangle has for its base the vertebral column, for its lower side the beginning of flatness, for its upper limit the beginning of dulness. The triangle represents the retracted or compressed lung which may be apposed to the chest wall in this region. Its recognition is important for the correct determination of the upper limit of the effusion. The tympanitic note above the layer of fluid may change in pitch with the mouth opened and closed (Williams' tracheal tone) during inspiration and expiration (Friedreich's phenomenon), and on changing the position of the patient (Gerhardt's phenomenon). A cracked-pot sound also may be heard in the absence of cavity.

With right-sided effusion, the dulness merges below with that of the liver. On the left, the tympany from inflation of the stomach with gas may be confusing and mask slight changes in the note from fluid. With considerable fluid in the left pleura, the normal tympany of the semilunar space between liver and spleen (Traube's semilunar space) may be obliterated.

Curved Line of Flatness with Pleural Effusions.—The limitation of fluid by dulness by some observers, and flatness by others is responsible for much confusion in the description of the line assumed by the upper border. If the dull triangle mentioned above be included, the upper limit is nearly horizontal behind. With a small or medium effusion, only the line of flatness should be regarded as indicating its upper limit. Ellis, of Boston, correctly traced the curve, which Garlaud¹ verified clinically and explained by a series of experiments. With small or medium effusions, its general shape is that of an elongated "S," lowest behind, advancing upward and forward to the axillary region, where it is highest, thence sloping gradually downward. With large effusions the curve may be flattened to assume a more nearly horizontal line. The curves of the line of flatness correspond to the line of apposition between the lower border of the lung and the pleural fluid. The curve may be of diagnostic value as a confirmatory sign of pleural effusion.

Shifting Dulness.—Dulness due to pleural effusion shifts on changing the position of the patient. This is especially true of small and recent effusions. With the patient upright, then in the horizontal position the upper border of fluid changes its level. It is absent in the presence of encapsulating adhesions and may be slight or absent with large effusions. Due allowance must be made for normal changes in the percussion note over the chest in different positions. The posterior-inferior parts, where the test is usually made, normally become more resonant when the patient assumes a horizontal position, as in bending forward or lying face downward. The maintenance of one position during the development of an effusion is capable, to a certain extent, of modifying the location of the

¹ *Boston Med. and Surg. Jour.*, September 17, 1874; *Pneumono-dynamics*, Boston, 1878.

fluid. If the patient has been constantly on his back, the upper limit of fluid is likely to be higher behind, and small effusions may be confined to the back and posterior axilla. It should be remembered in testing shifting dulness that the fluid may change its position only slowly. A slight shift in dulness is difficult to determine and of practically no value in diagnosis.

Sense of Resistance.—In addition to the lack of resonance or other peculiarities of the percussion note appreciated by the ear, the lack of vibration and sense of resistance are apparent to the finger as well.

Auscultation.—Early in the disease, a friction rub may be heard. Its presence does not exclude fluid between lung and diaphragm or in the neighborhood of apposed pleural surfaces. With small effusions, the rub not infrequently persists in the lower anterior or lateral portions of the chest. The disappearance of this sign as fluid accumulates is probably due not so much to intervention of fluid between lung and chest wall as to the mechanical obstruction to the expansion of the lung. The reappearance of friction in cases with pleural effusion is favorable, indicating diminution or disappearance of fluid, provided extension of fibrinous pleuritis to previously uninvolved parts be excluded.

Crepitation, resembling that in the early stage of lobar pneumonia, and audible at the base of the lung, may also be heard in cases which later develop demonstrable fluid. Its explanation is not clear. It may be ascribed to fine pleural friction, to air entering fluid in alveoli underlying an inflamed pleura, and to expansion, during inspiration, of a slightly retracted and atelectatic lung, giving rise to crepitation coincident with the separation of previously apposed alveolar walls. A similar sound may also be heard at the termination of the disease, and may indicate that the pleural layers are again approximated, or that air is again admitted to the base of the lung.

Breath Sounds.—Changes in the breath sounds in uncomplicated pleural effusion are due to several factors, more than one of which usually operate in any given case. They depend on diminished expansion of the lung, from spasm or paralysis of the respiratory muscles, to changes in the lung itself from retraction or pressure, and to the presence in the pleural cavity of fluid which modifies or may even abolish the vibrations conducted from the lung to the chest wall.

Early in the disease irritation of the pleura and pain diminish the respiratory murmur from spasm of the respiratory muscles and fixation of the side. In the presence of fluid, however, the retraction and increased density of the lung may give rise not only to a diminution in the intensity of the respiration, but to a change in its character. With small effusions, the inspiration is merely diminished, while expiration is abnormally long, somewhat higher pitched, and slightly bronchial in character. As the fluid increases the breathing over the base of the lung may have a distinctly tubular quality. This is often most marked in the interscapular region above the level of the fluid. With large effusions the breathing is vesicular in the upper part of the chest. It may be bronchial above and absent below the level of the fluid. When the lung is completely retracted and compressed, there may be almost no respiratory murmur over the

affected side. At times the breathing may have an amphoric character in the upper part of the chest. Rales, as well as bronchial breathing, may have a metallic quality and thus suggest cavity. In children the breathing is more likely to be bronchial than in adults. With the subsidence of the effusion the vesicular breathing returns, but may for long or even permanently remain somewhat diminished. As the atelectatic lung expands, rales can usually be heard. An accompanying catarrh or œdema of the lungs may give rise on the side of the effusion, to rales which may have a consonating quality from pulmonary compression. The breathing over the unaffected lung is often increased with prolongation of expiration.

Voice Sounds.—The voice sounds are often increased above, diminished or absent below the level of the fluid. The voice usually has a peculiar nasal or bleating quality, the so-called ægophony. It is most often heard in the posterior and lower thoracic regions. The whisper is variable, but in general is increased over the region where bronchophony is heard, and may have a bronchial character. It is usually diminished or absent over the fluid.

EXAMINATION OF THE HEART.—Dislocation of the heart is an important sign of pleural effusion. The position of the visible cardiac impulse should be noted. Palpation for the systolic impulse in the spaces on either side of the sternum may furnish more definite information. In some cases pulsation can be neither seen nor felt, and reliance must be placed on auscultation.

Special Physical Signs.—1. **DISPLACEMENT OF THE HEART.** (a) *Away from the Affected Side.*—Provided the heart is free to move laterally, its displacement is an important sign of an accumulation in the pleural sac. The intrapleural pressure on the diseased side need not be actually positive. Apposition of fluid or other material to the heart is not a necessary factor. Because of the normal position of the heart on the left, it is always displaced a great distance to the right with left-sided pleural disease than to the left with disease of the right pleura. To judge from Carrière's observations and experiments, the amount of fluid in the left chest may reach 700 cc. without displacement of the heart. The writer has seen slight cardiac displacement develop under observation in a girl of fourteen, from whose left pleura 250 cc. of pus were evacuated by operation. Cardiac dislocation may be noted before dilatation of the side is evident. As much as 1000 cc. of fluid may be present in the right pleura without evident displacement of the heart to the left. In such diseases as pneumonia, in which pleural fluid may occur as a complication, or in cases in which its presence is suspected, a careful record of the position of the heart may be of unexpected value later, when slight deviation from its originally recorded position may be a deciding factor in a diagnosis, otherwise doubtful because of pulmonary changes complicating the physical signs. Since cardiac displacement depends not only on a loss of retractile force in the lung on the diseased side, but also on the maintenance of elastic tension in the opposite lung, any interference with the latter from disease will correspondingly limit the cardiac excursion toward that side.

(b) *Toward the Affected Side.*—Occasionally in the course of long-continued pleural disease, absorption may lead to an increase of negative pressure on the diseased side. The heart may then be pushed toward this side by the relatively greater but still negative pressure in the unaffected pleura. The heart may be displaced toward the side of an effusion in consequence of massive collapse of the lung on the side corresponding to the effusion. Thus far mention has been made only of cardiac displacements from differences of intrapleural pressure. The heart may, however, actually be pulled to one side by the contraction of adhesions between it and neighboring structures.

(c) *Position of the Displaced Heart.*—The heart practically always maintains its position with the apex to the left of the base, pulsation to the right of the sternum arising at the base of the heart. In Lafforgue's¹ case, however, with a large effusion of blood in the left pleural sac, the heart was found at autopsy pointing to the right.

2. DIAPHRAGM PHENOMENON.—The sign is of value in unilateral pulmonary or pleural disease. It is absent in pneumonia of the lower lobes, is diminished in amplitude or absent and abnormally low in the presence of pleural fluid or air.

3. PARAVERTEBRAL TRIANGLE OF DULNESS.²—The presence of a normal triangle of dulness at either side of the spinal column in the inferior thoracic region makes the pathological triangle more difficult of interpretation and somewhat limits its diagnostic value.

Having determined the limits of a suspected effusion by percussion and similarly outlined the lowest limit of pulmonary resonance on the unaffected side, the spinous processes of the vertebræ are percussed from above downward and the point noted where relative dulness begins. This usually corresponds to the level of relative dulness on the affected side, and somewhat higher than the level of flatness. Percussion of the unaffected lung in horizontal lines toward the spinal column discloses a paravertebral area of relative dulness of a triangular shape. The vertical side of the triangle coincides with a line drawn through the spinous processes of the vertebræ, the base with the limit of pulmonary resonance on the sound side. Its outer side is formed by a line extending obliquely downward and outward. The height of the vertical and the width of the base line vary with the size of the effusion. On changing the position of the patient from the upright to the horizontal, the dull triangle nearly or quite disappears unless the fluid is encapsulated. The respiratory murmur, the voice sounds, and fremitus are diminished over this area, but the changes are less marked than on the affected side. The character of the fluid appears not to influence the triangle.

The dull triangle is practically constant in the presence of free pleural fluid or of encapsulated fluid in contact with the spinal column. The sign is of little or no value in the diagnosis of small effusions. An appreciation

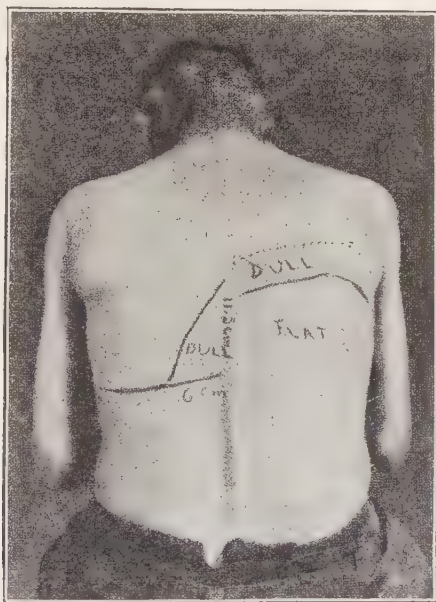
¹ *Gaz. d. hôp.*, 1902.

² The triangle was first noted by Korányi in 1897 (in the fourth volume, p. 717, of *Belgógyászati Kezikönyze*, and again in Eulenberg's *Realenzyklopädie der gesamten Heilkunde*, vol. 13). It was independently rediscovered and more fully described by Grocco (*Riv. crit. di clin. med.*, Firenze, 1902).

of its presence in connection with unilateral effusions enables the examiner to avoid the mistake of regarding dulness in the opposite paravertebral region as an indication of important pulmonary or pleural changes in this part of the thorax. It is of importance in the differential diagnosis of pleural effusion and subdiaphragmatic abscess, being present in the former and absent in the latter. (See Subdiaphragmatic Abscess p. 246).

In explanation of the phenomenon Baduel and Siciliano¹ suggest that fluid intervening between the spine and resonant lung inhibits the capacity of the former for sonorous vibrations, thus acting as a mute. The diminished resonance extends into the paravertebral region and increases in width from above downward, since the fluid at its base comes into wider

FIG. 8.



Aortic insufficiency; hydrothorax on the right side; paravertebral triangle of dulness on the left. (Thayer and Fabyan.)

contact with the spinal column and extends farther toward the opposite side. Displacement of the mediastinal contents and compression of the sound lung may play a part in its production.

Paravertebral Dulness on the Affected Side.—Free pleural effusions distend the pleural sac and interrupt spinal vibrations with the production of dulness on one or both sides of the spine according to the size of the effusion. If the effusion is small, the dulness may be limited to the paravertebral region on the affected side without evidence of Grocco's triangle on the other. With pneumonia affecting the lower lobes and uncomplicated by an effusion, on the other hand, a zone of

¹ *Riv. crit. di clin. med.*, Firenze, 1904, 5, 5, 21, 37.

relative resonance about two fingers' breadth in width can usually be demonstrated in the paravertebral region on the affected side.¹ This strip of relative resonance may be obvious only in the presence of extensive lobar pneumonia and absent or doubtful with small areas of consolidation from other causes. It is probably due to uninterrupted spinal vibrations of the unaffected lung. A zone of dullness in the paravertebral region on the affected side with pleural effusion and relative resonance in this region, with lobar pneumonia is of value in differentiating the two conditions.

Blood.—The number of red cells and the amount of hemoglobin present no striking features beyond usually not more than slight grades of secondary anemia.

White Cells.—In general, it may be said that the leukocytes in primary serofibrinous pleuritis are only rarely above normal in the absence of complications. Infectious pleuritis, on the other hand, is usually accompanied by leukocytosis. The white count, therefore, may be of value in distinguishing the two forms of the disease.

Tuberculous Effusion.—Of 33 cases of primary serofibrinous pleuritis in which tubercle bacilli were found in the fluid by inoculation the white count was above 12,000 in only 3 (9 per cent.). In 301 primary cases, of probable tuberculous nature, the white count was 12,000 or over in 57 (18.9 per cent.).

Infectious (Non-tuberculous) Pleuritis.—The *metapneumonic* effusions, are, as might be expected, accompanied by an increase of the white cells. Of 28 cases in this class the leukocytes were above 12,000 in all but 6 (78.5 per cent.).

Axillary Glands.—Rarely the axillary glands on the affected side may be enlarged by extension of the pleural disease, whether simple, tuberculous or malignant.

Inequality of the Pupils.—This may in rare instances occur from involvement of the sympathetic nerve. The difference in size is usually slight.

Blood-pressure.—This is usually normal with pleural effusions. Capps² noted an increase of blood-pressure during the excitement preceding thoracentesis. There was a constant fall during the withdrawal of the fluid, the average in 19 observations being 20 mm. Hg. Evacuation of large amounts of fluid, rapid withdrawal, long duration of the effusion and senile changes in the bloodvessels and heart, increased the fall of pressure.

Radioscopy.—This may confirm the results of physical examination, showing the limits of the effusion, the position of the displaced heart and the diaphragm. It may also show the presence of unsuspected pulmonary processes. It is especially valuable in locating an encapsulated effusion. The fluoroscope admits of examination from different points of view in rapid succession, but the radiograph is, in general, to be preferred. The plates are most satisfactory if the patient can hold his breath during the exposure. Pleural adhesions may be suggested by a lack of diaphragmatic excursion. Thick pleura without fluid may be indicated

¹ Lord: *Boston Med. and Surg. Jour.*, 1914, **170**, 245.

² *Jour. Am. Med. Assn.*, 1907, **48**, 22.

by a lack of uniformity, by irregular limitation of the shadow and an absence of depression of the diaphragm and dislocation of the heart. The shadow is less dense than with fluid. In the presence of pleural fluid, the shadow is more uniform, more sharply outlined, and when the fluid is free occupies the lower part of the pleural space. Its upper border is curved and highest in the axillary region unless pneumothorax is present, when it assumes a hydrostatic level. A comparison of plates taken with the patient upright and lying down confirms the clinical observation of the mobility of fresh serofibrinous effusions. The shadow produced by serous is less dense than by purulent or hemorrhagic fluid.

Complications.—Lesions having an etiological relation with the disease have been considered. It is difficult oftentimes during life or even at the postmortem table to separate them from conditions dependent on the pleuritis. These secondary processes only need be considered here. Tuberculosis may rarely extend from pleura to uninvaded lung. The progress is usually, however, from lung to pleura. Acute miliary tuberculosis may rarely complicate or follow serofibrinous effusion. Infection may extend to the opposite pleura, the pericardium, peritoneum, or other parts of the body. Perihepatitis or perisplenitis may thus arise. Thrombosis of the pulmonary vessels, the venæ cavæ, heart, iliac, femoral, saphenous, or other veins may be associated with increased intrathoracic pressure and infection. Embolism may be rapidly fatal. Œdema of the lungs is a constant danger in large accumulations and with untapped effusions is probable due to cardiac insufficiency. Perforation of the lung or thoracic wall complicates purulent effusions with unfortunate frequency but is rare with the serofibrinous form. Serous expectoration without relation to thoracentesis has been noted by Scriba,¹ Sahli,² and Appel.³ Nephritis probably bears only a chance relation to pleuritis. It arose under observation in only 1 of 500 cases in the writers' series.

Causes of Sudden Death.—Death may be due to associated and independent lesions to which the pleuritis is secondary. Such causes need not be considered here. Of causes dependent on the serofibrinous effusion, thrombosis and embolism are among the most frequent. The pulmonary vessels, the auricles, the venæ cavæ, iliac and femoral veins often contain thrombi, which may give rise to emboli, with rapidly fatal pulmonary embolism, as in 5 of 14 autopsies in this series. Cerebral embolism is less common. Œdema of the lungs may be the only associated lesion found, as in one case with a double effusion. Postmortem examination does not always disclose the immediate cause of death, which has then been thought to be due to compression of the aorta (Trousseau), or to a kink or twist in the inferior vena cava (Bartels), but Osler in a number of observations was unable to substantiate the latter. Cerebral anemia, from a mechanical hindrance to the circulation, is a possible cause. Pressure on the venæ cavæ, and the heart itself, especially the auricles, may embarrass the cardiac mechanism, resulting not only in cyanosis, rapid, feeble pulse and dyspnoea, but even syncope and death. Various factors may operate in

¹ *Deutsch. Arch. f. klin. Med.*, 1886, **36**, 329.

² *Mitth. a. klin. u. med. Inst. d. Schweiz.*, 1894.

³ *München. Ann.*, 1897, Fall, 15.

individual cases. Large double or left-sided effusions are more dangerous. Death may follow sudden changes of position, an attack of pain, deep respiration, or a paroxysm of cough.

Duration.—Of 369 cases of primary serofibrinous pleuritis, the time from the beginning of symptoms to discharge from the hospital was less than three weeks in 53, three to six weeks in 167, six to nine weeks in 60, nine to twelve weeks in 43, three to six months in 31, six months to one year in 12, two years or over in 3. Thus, about 60 per cent. ran their course within six weeks, about 87 per cent within three months. The duration is longer with large effusions, in old and debilitated patients, in the presence of complications, in untapped cases or those in which evacuation is delayed. It is shortest in primary effusions, in young and otherwise apparently healthy individuals, treated by early tapping.

Relapse.—Although it is not uncommon after withdrawal of fluid for it to reaccumulate under observation and necessitate one or more tapplings, it is rare for a serofibrinous effusion to reappear on the same side after it has been fully absorbed or removed. The obliteration of the pleural sac following serofibrinous effusion is probably responsible for the rarity of true relapse.

Sequelæ.—It is rare for serofibrinous effusions to change from serous to purulent fluid. Of 1185 cases, empyema developed in only 16 (1.3 per cent.). When empyema follows serofibrinous effusion, the fluid has usually been turbid, with an excess of polynuclear cells from the beginning. Spontaneous or artificial pneumothorax may occur, and, if the communication is through the lung, infection may follow. Imperfect technique in tapping may cause empyema. Slight dulness, diminished expansion, breathing and fremitus last for a variable period after the disappearance of serofibrinous fluid. The intercostal spaces may be slightly narrowed and the affected side somewhat smaller. These changes may be permanent, but are less common and less marked than after empyema. The heart usually returns to its normal position. Rarely it may be fixed by adhesions in an abnormal position toward the sound side or slightly displaced toward the affected pleura. Slight lateral deviation of the spine may accompany these changes.

Diagnosis.—This is usually easily made from the onset with pain, the diminution or disappearance of which is accompanied by increasing dyspnoea, diminished expansion of the affected side, initial narrowing, with later enlargement of the side and widened interspaces, the character and distribution of the dulness, diminished or absent breathing and fremitus, and the displacement of neighboring organs.

DISEASES WITH WHICH AN EFFUSION MAY BE CONFUSED.—1. *Intra-thoracic.* (a) *Thick Pleura.*—Following the partial or complete absorption or removal of pleural fluid, the thickened pleura may give rise to some confusion. There may be slight dulness, diminished breathing and fremitus. The side is not flat, however, the breathing only slightly altered, without bronchial character, agophony is absent, and the fremitus although it may be diminished, is not absent. The paravertebral triangle of dulness opposite the affected side is absent and the heart is not displaced.

(b) *Pneumonia*.—Typical lobar pneumonia is easily differentiated by its more severe onset, with chill and rapid rise of temperature, cough with rusty sputum, dullness (not flatness), bronchial breathing, increased voice, whisper and tactile fremitus, and consonating rales. The signs are often confined to parts or the whole of one or more lobes. Atypical pneumonia may closely simulate effusion. Cough and expectoration may be absent. Partial or complete involvement of the lower lobes with occlusion of the bronchi by secretion (massive pneumonia) may give rise to signs of effusion. If the bronchi can be emptied by cough, the signs of pneumonia may then become clear. The absence of cardiac displacement is important. A narrow strip of relative resonance in the paravertebral region on the affected side with lobar pneumonia and dullness in this region with pleural effusion is of some value in differentiating the two conditions.

(c) *Tumors of the Lung and Pleura*.—Tumors which reach the periphery of the lung may give rise to some confusion. There may be flatness, diminished or absent breathing and fremitus. The site and contour of the process may differ from pleural fluid. Bloody sputum, dyspnoea, stridor, paralysis of the vocal cords, dysphagia, dilatation of the cervical or thoracic veins and superficial metastases may be suggestive. If the pleura is invaded by the new growth, an effusion is common and this may mask the pulmonary process. Exploratory puncture may evacuate bloody fluid. Echinococcus of the lung or pleura may simulate serofibrinous pleuritis.

(d) *Pericarditis with Effusion*.—This may offer some difficulty of differentiation from an encapsulated pleural effusion in the left antero-lateral region. The same symptoms of pain, cough and dyspnoea may be present in both conditions, and on inspection the left side of the chest may show restricted expansion. Dullness or flatness, diminished or absent respiration, voice, whisper and tactile fremitus may be present over the left antero-lateral part of the chest. The following features, however, may serve to suggest pericardial rather than pleural effusion: a history of rheumatic fever preceding or accompanying the onset of the attack, a greater degree of cyanosis than might be expected with pleural effusion of similar size, dilated cervical veins, paradoxical pulse, feeble or absent cardiac shock, dullness beyond the limit of palpable cardiac impulse to the left, a pyriform or oval contour to the dull area with dullness at the left of the sternum as high as the second rib, declining sharply toward the left axillary region, pericardial friction and feeble heart sounds. With large pericardial effusions and especially those which distend the posterior part of the pericardial sac important signs may be present in the left back in the region of the angle of the scapula. Over an area of variable size in this region there may be dullness, bronchial breathing, agephony, and increase of voice and whisper. The tactile fremitus is likely to be diminished. If the heart is held to the chest wall in front by adhesions, pericardial friction may be present and the effusion may readily be overlooked. The patch in the left back is often mistaken for pneumonia or pleural effusion. Careful percussion will, however, demonstrate that the dull area does not reach to the base of the lung. Similar findings in the

back may be found in children with much enlarged hearts and without pericardial effusion. Examination by means of the roentgen-rays may be of great value in the differentiation.

2. *Abdominal Affections.*—Subdiaphragmatic abscesses and tumors, especially echinococcus cysts, may simulate an accumulation of pleural fluid. Abdominal pain, tenderness and muscular spasm may be due to diaphragmatic pleurisy.

Subdiaphragmatic abscess may present special difficulty of differentiation. Preceding abdominal symptoms may suggest the possibility of abdominal suppuration. Among the numerous causes, appendicitis, pyelephlebitis, hepatic abscess in connection with cholangitis with or without gall-stones, tropical abscess and actinomycosis, perforated gastric or duodenal ulcer, suppuration in or about the pancreas, salpingitis and disease of the kidney or spine may be mentioned. In some cases preceding abdominal symptoms are lacking. Cough and expectoration are likely to be absent. The right side is more often affected than the left. The diaphragm may be elevated far into the chest or intrude only slightly into the lower thoracic aperture. In cases uncomplicated by pleural effusion, the dome-like elevation of the diaphragm may be outlined on percussion as a dull area at the base of the lung with convex upper margin. Grocco's paravertebral triangle of dullness is absent. An important feature in the percussion outline is the maintenance of resonance on the affected side in the paravertebral region which is dull in the presence of free pleural effusion. Over the dull area the breathing is diminished and may have a bronchial quality from pulmonary retraction or compression. The voice sounds are diminished, and may have an ægophonic quality. The tactile fremitus is diminished or absent. A friction rub may be heard if fibrinous pleurisy is present. The heart is less displaced than with pleural effusion of corresponding size. If a complicating pleural effusion is present, the signs are those of this condition. Exploratory puncture may demonstrate the presence of pus. Serofibrinous fluid may be obtained from the pleura and pus from below the diaphragm. Inspiratory depression of the point of the needle may indicate that the diaphragm has been perforated. If the respiratory changes of tension are noted, an increase of pressure may be demonstrated during inspiration and a diminution of pressure during expiration. Roentgen-ray examination furnishes the most important evidence. By this means an abrupt dome-like elevation of the diaphragm may be seen as a dense shadow with convex upper border at the base of the lung (Fig. 9). In the absence of a complicating pleural effusion a clear space is observed at the costophrenic sinus and toward the mid-chest. Fluoroscopic examination usually shows diminished inspiratory depression and expiratory elevation of the diaphragm as with pleural effusion. If a complicating pleural effusion is present the roentgen-ray picture is obscured, but the outline of the elevated diaphragm may still be seen through the shadow caused by the effusion.

Although I have had the opportunity of observing a considerable number of subdiaphragmatic abscesses and have repeatedly warned students of the dangers of a mistaken diagnosis, I have myself erron-

cously regarded a collection of pus below the diaphragm as empyema in two instances. Operation produced open pneumothorax which might have been avoided if the preoperative diagnosis of subdiaphragmatic abscess had been made. The cases are so strikingly an example of the necessity for roentgen-ray examination that a brief account of the clinical aspects in one of them may serve to prevent similar errors. In the first case, seen in 1914 at some distance from Boston, a married woman gave a history of sore throat, stitch in the right side, chilliness and slight cough without sputum for three days and fever for about thirty-six hours. There was dullness at the right base as high as the angle of the scapula with abrupt decline of its upper margin toward the spine and the posterior

FIG. 9



Subdiaphragmatic abscess of the right side. The dome-like elevation of the diaphragm is indicated as an opaque shadow with convex upper margin at the base of the right lung. The costo-phrenic sinus is obscured by a slight accumulation of pleural fluid. (Massachusetts General Hospital, No. 191899.)

axillary line. Grocco's triangle was absent and the paravertebral region on the affected side was noted to be more resonant than was to be expected with free pleural effusion. The breathing was diminished and bronchial over the dull area, with increased and bronchial whisper, agophony, absent tactile fremitus and numerous, fine consonating rales. The heart was displaced slightly to the left. The white count was 73,000. About one liter of cloudy fluid containing streptococci was aspirated from just within the thoracic wall by puncture in the seventh space in the angle of the scapula line. The condition was interpreted as encapsulated empyema, but operation showed the pleura to be free and the pus to be below the diaphragm. Roentgen-ray examination would probably have shown a dome-like elevation of the diaphragm and free costo-phrenic

sinus, thus suggesting subdiaphragmatic abscess, but no portable apparatus was then available. Greater importance should have been attached to the absence of Grocco's triangle and the presence of only slight cardiac displacement with such an accumulation of fluid.

DETERMINATION OF THE CHARACTER OF PLEURAL FLUID.—This is impossible in most instances without exploratory puncture, but certain suggestive features may be mentioned. *Hydrothorax* is most easily distinguished from the presence of cardiac or renal disease or both, bilateral fluid, which shifts more readily on changing the position of the patient, and œdema elsewhere, as well as absence of pain, fever, leukocytosis and friction rub. In unilateral hydrothorax without general dropsy, the distinction may be impossible. *Hemorrhagic fluid* may be suspected following trauma, when the effusion is secondary to malignant disease, or with an eosinophilia in the circulating blood. *Chylothorax* can hardly be distinguished, but may be suspected with the known presence of chylous ascites. *Empyema*, in typical cases, may be differentiated. It is more likely to be secondary and metapneumonic, while serofibrinous effusion is much more likely to be primary. If the patient is a child and under five years of age, the chances are much in favor of pus. The symptoms are of little assistance in individual cases, but in general are more severe in empyema, with higher and more irregular fever, chills, sweats, and more rapid loss of flesh, strength and color. Œdema of the skin, dilatation of the superficial veins, thoracic pulsation, perforation of the lung or other organs may suggest empyema. A leukocytosis above 12,000, unexplained by other features, suggests an infectious process and usually means pus.

Exploratory Puncture.—This may be done without pain as follows: The site of the puncture is frozen with ethyl chloride spray. The syringe¹ is filled with about 2 cc. of 2 per cent. novocaine solution with 0.002 per cent. epinephrine and the needle introduced through the frozen area. The needle is thrust inward by degrees, perpendicular to the surface, each advance being preceded by the injection of a small amount of the fluid into the tissue in front of the point. The rib is passed close to the upper margin to avoid the intercostal artery. After the pleural sac is reached, the syringe should still contain some fluid which may then be used to dislodge from the lumen of the needle any fibrin or other material preventing aspiration. Thick pus may fail to flow through a small needle.

In addition to the determination of fluid, the operator may appreciate any unusual thickness or density of the pleural or pulmonary tissue by the amount of resistance encountered by the instrument (palpatory puncture). In rare instances a diagnosis between pleural and subdiaphragmatic fluid may be made. By the removal of the syringe and the attachment of a rubber tube to the needle, the apparatus is converted into a siphon and the amount of pleural pressure may be determined, as suggested by Krönig. The normal depression during inspiration and elevation during expiration of the column of fluid may be reversed in sub-

¹ The same apparatus is used both for exploratory puncture and aspiration.

diaphragmatic collections. The withdrawal of small amounts of fluid by exploratory puncture is occasionally followed by rapid spontaneous absorption of what remains.

In rare instances, if the needle is used for exploratory puncture, the microscopic examination of a piece of tissue caught in the lumen may furnish the diagnosis. In one of my series a tubercle was thus demonstrated. Prentiss¹ made the diagnosis of sarcoma and Steele and Girvin² of carcinoma of the pleura by this means.

EXAMINATION OF PLEURAL FLUIDS.—Under normal conditions there is merely enough pleural fluid to lubricate the apposing surfaces of the pleuræ; and no chemical analysis of this has been made.

1. *Chemistry*.—Pleural fluid may be *serous*; it may contain varying amounts of fibrin, when it is known as *serofibrinous*; it may also vary in its contents of blood and pus and may then be termed *hemorrhagic*, *fibrino-purulent*, or *purulent*. The presence of chyle justifies the term *chylous*; of fat not due to chyle, *chyliform*.

Transudates and Exudates.—It is customary to make a clinical distinction between fluids resulting from hydremia and stasis or transudates and those arising in the course of inflammatory processes or exudates. In general, transudates are of relatively low specific gravity and contain a small amount of albumin, *i. e.*, a specific gravity of 1010 or under for hydremic fluids, with traces to 1 per cent. of albumin; and 1010 to 1015 in venous transudates, with 1 to 3 per cent. of albumin. The albumin is principally serum albumin, serum globulin, and a trace of fibrinogen. Only a very slight precipitate follows the addition of a few drops of acetic acid to the fluid. It coagulates slowly or not at all, unless mixed with blood. The specific gravity of exudates, on the other hand, is usually 1018 or higher, with 4 per cent. or more of albumin. They show a more abundant precipitate on the addition of acetic acid, contain a larger amount of fibrinogen, and usually coagulate rapidly with or without the presence of blood. For the estimation of albumin Esbach's test may be used, but is only approximately accurate, and for more exact determination more complicated methods must be employed, such as the weight of the precipitated proteid or the total nitrogen (Kjeldahl).

2. *Cytology*.—*Cytodiagnosis*.—*Technique*. The fluid should be examined as soon as possible after withdrawal. To prevent spontaneous coagulation and the entanglement of cells in the meshes of fibrin, it may be placed at once in a sterile flask containing about one-third to one-half its volume of 1 per cent. sodium citrate in 0.85 per cent. salt solution. If coagulation has already occurred, Widal recommends agitation with glass beads to dislodge entangled cells, but such a procedure may give less accurate results than the examination of fluid in which clotting has not taken place. The sediment is obtained by centrifugalization, the supernatant fluid carefully decanted, and thin smears made with the platinum loop. These are allowed to dry in the air or over a flame. Care must be taken not to burn the preparation. Wright's³ blood stain is

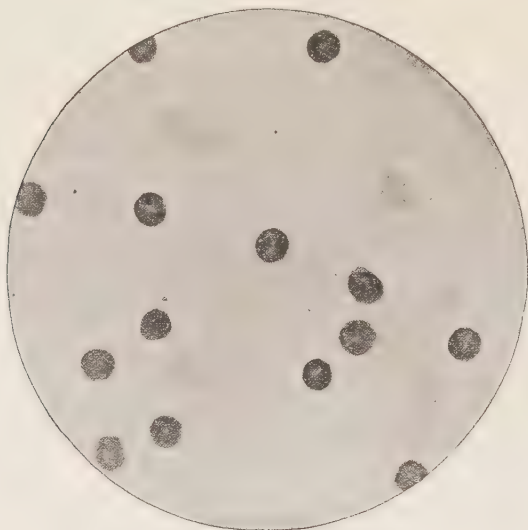
¹ *Trans. Assn. Am. Phys.*, 1893, **8**, 191.

² *Proc. Path. Soc.*, Philadelphia, 1901, p. 164.

³ *Jour. Med. Res.*, January, 1902, p. 138.

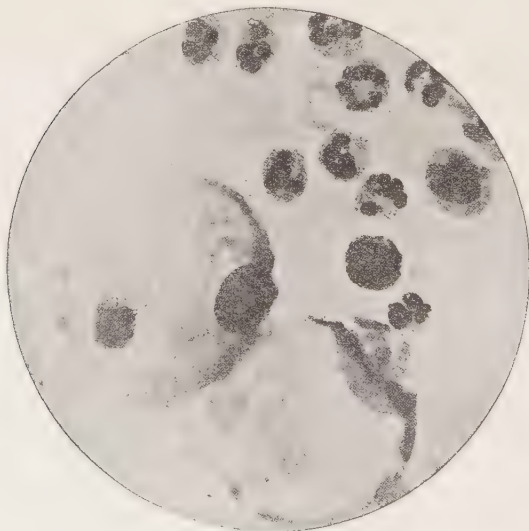
allowed to remain on the cover-glass from one-half to one minute, then diluted with 8 to 10 drops of water, and allowed to stand one to two

FIG. 10



Lymphocytosis. Case of primary tuberculous pleurisy. $\times 750$. (Musgrave.)

FIG. 11

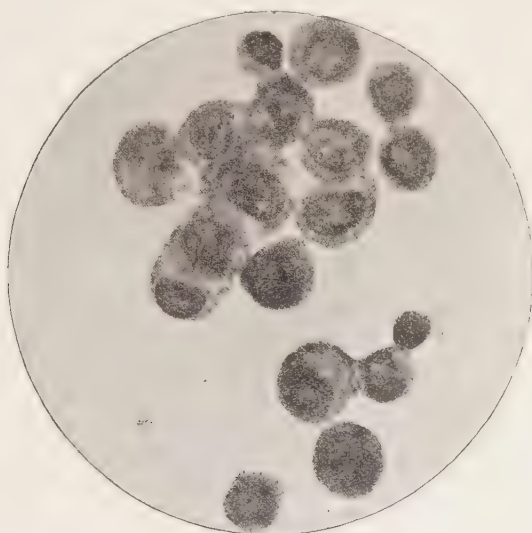


Large phagocytic endothelial cells and polynuclear leukocytes. Case of acute infectious pleurisy. $\times 750$. (Musgrave.)

minutes. The preparation is washed in a gentle stream of tap water, dried over a flame and mounted in balsam.

Polymorphonuclear neutrophiles correspond to similar cells found in the circulating blood. Eosinophiles are often found in small numbers, mast-cells less often. The lymphocytes correspond to similar cells in the blood. Endothelial cells are large, flat, irregular, round, or oval in contour, with a round or oval blue nucleus, which is poor in chromatin and often vacuolated. They may be isolated or in plaques, the so-called "Placards endothéliaux." Unfortunately, between typical examples of lymphocytes and endothelial cells there are atypical forms of mononuclear leukocytes which cannot be fairly classed with either of the two groups. Such atypical cells, however, usually comprise but a small proportion of the white cells, and may thus introduce a negligible error in the differential counts. In some cases, the classification of the cellular elements is impossible because of degenerative changes.

FIG. 12



Endothelial plaques and cells. Case of hydrothorax due to cardiac disease. $\times 750$.
(Musgrave.)

Cytologic Formulæ.—Widal¹ stated that (1) a predominance of polymorphonuclear leukocytes means an effusion of infectious origin (pneumococcus, streptococcus, staphylococcus); (2) of lymphocytes, a tuberculous effusion; and (3) of endothelial cells, especially if in plaques or sheets, an effusion of mechanical origin. Recent observations make it probable that the character of the cells in pleural fluids depends not only on the cause of the process, but also on the intensity of the pleural reaction. The predominance of one type of cell, therefore, cannot be regarded as a specific indication of an infectious, tuberculous, or mechanical origin. An excess of polymorphonuclear leukocytes in infectious pleuritis is subject to least variation. A transient excess of polymorphonuclear neutrophiles

¹ Widal and Ravaut: *Compt. rend. Soc. de biol.*, 1900, p. 648

has been found by Widal and others in early pleural tuberculosis. The secondary infection of a pleura already the site of tuberculosis may likewise modify the character of the cellular elements, with an increase in the relative proportion of polymorphonuclear cells. In mechanical effusions, it has been noted that they are relatively most numerous in the early stages of the disease. In long-standing transudates, lymphocytosis has been present without a reaction to tuberculin and in transudates shown by autopsy not to be tuberculous. As in fluids with lymphocytosis, so, also, in those with an excess of endothelial cells, an infection may raise the number of polymorphonuclear cells.

In malignant disease of the pleura, the cellular elements conform more nearly to those found in mechanical effusions, with an excess of endothelial cells, but large numbers of spindle cells may suggest sarcoma, as in Warthin's case. Examination of the fluid in conjunction with the history and physical examination may confirm an otherwise doubtful diagnosis.

3. *Bacteriology*.—For the demonstration of the pneumococcus, the pyogenic cocci, and other organisms capable of cultivation, smear preparations should be made and suitable media inoculated.

Animal Inoculation.—All instruments must be sterilized. Intraperitoneal inoculation of guinea-pigs is most successful. For the demonstration of tubercle bacilli, large amounts of fluid must be injected, but in divided doses. If the animal lives, three months should be allowed to elapse before the examination is made. Le Damany¹ made injections each week of 10 to 50 cc. of fluid, varying the amount according to the toxicity of the fluid, and was thus able to inoculate as much as 300 cc.

Prognosis.—In general, the immediate prospect in serofibrinous pleuritis is good. Large or double effusions, however, may be suddenly fatal. Of 500 cases in the writer's series, 4 (0.8 per cent.) died without other obvious cause than the effusion. In 1, large amounts of fluid rapidly reaccumulated, conforming to the uncommon variety known as pleuritis acutissima. No autopsy was obtained. The 3 remaining patients were not tapped. Two had double effusions, in one of whom autopsy showed that death was due to pulmonary embolism; in the second no other cause of death was found postmortem than œdema of the lungs. In the last patient there was a large unilateral accumulation, and examination after death showed pulmonary embolism. If an infectious and non-tuberculous cause can be established, the prognosis is favorable.

Prophylaxis.—In a large majority of the cases this embraces measures for the prevention of infection with the tubercle bacillus and other organisms.

Treatment.—1. **THE NATURAL OR SPONTANEOUS CURE.**—That large proportion of cases coming to autopsy with pleural adhesions, associated with fibrocaseous or calcified pulmonary lesions, shows that pleural disease, directly or indirectly dependent on the tubercle bacillus, is frequently arrested or healed. Tuberculous nodules in the pleura, as elsewhere, may be walled off by a dense envelope of fibrous tissue, and thus

¹ *Presse med.*, November, 1897, p. 329.

prove of little danger to the individual, forming latent foci. Calcification may take place, as in 5 of 27 cases (M. G. H.), with obsolete tuberculosis as a result. Tuberculous granulations in a part or the whole of the pleura may finally be converted into firm, fibrous tissue, ending in obliteration of the pleural sac and no further trouble from the process. The clinical history of cases of certain or probable pleural tuberculosis shows that recovery is not infrequent.

2. GENERAL MEASURES.—For purposes of treatment, it is best to assume every case of primary serofibrinous pleurisy to be tuberculous, unless there is good reason to believe otherwise. Fortunately, many patients are still in fair health when they first come under observation. The course of the disease is often slow and spontaneous recovery frequent, which, indeed, too often fosters half-way measures in its care. As in tuberculosis elsewhere, we must rely chiefly on rest, fresh air and the improvement of nutrition.

The patient, should be frankly told the seriousness of the condition. We can otherwise hardly secure his acceptance of the necessary restrictions on his mode of life. The chances with primary serofibrinous effusion are about 3 or 4 in 10 that pulmonary or other tuberculosis will appear within a period of six or seven years. These figures have this hopeful aspect, however, that they are for the most part gathered from cases in which treatment terminated with the disappearance of the effusion. They probably, therefore, represent the natural evolution of the disease, and a longer or even a permanent arrest may be expected in patients who consent to more careful supervision and regulation.

The general management should be similar to that in active pulmonary tuberculosis. During the acute stage while there is fever absolute rest in bed should be maintained, but the rest treatment should not end with the subsidence of fever and disappearance of fluid. It has been my custom to continue to keep patients with primary pleurisy at rest in bed for a month after all indications of activity have subsided. During the second month somewhat greater latitude is permitted and during the third month greater freedom is allowed. Patients who have apparently fully recovered should be kept under observation and every effort made to maintain the nutrition at a high level. Indiscretion and neglect of this precaution may bring him again under treatment with pulmonary or other tuberculosis too far advanced for arrest. Loss of weight, fever, cough or other suspicious symptoms should receive immediate attention and if necessary a further course of rest, extra feeding and fresh air.

3. LOCAL APPLICATIONS.—These are for the alleviation of symptoms. The ice-bag, hot-water bottle, and hot applications repeated every two hours may efficiently relieve pain, for which, however, morphine may be necessary. Strapping the affected side further displaces the lung and other organs. It may actually hinder absorption by compressing the lymph channels.

4. SPECIAL MEASURES.—*Thoracentesis*.—*Indications*.—In general, the opinion of the present time is in favor of tapping serofibrinous effusions (1) with pressure symptoms, such as severe dyspnoea, cyanosis, or rapidly developing cardiac weakness; (2) of large amount, with dislocation of

heart and mediastinum, even without pressure symptoms; and (3) of medium amount when other means have failed to bring about absorption and two or three weeks have elapsed.

With *pressure symptoms and large effusions, thoracentesis is imperative* and should be done without delay. It has been the unfortunate experience of many physicians to decide on evacuation in such cases within a given time, before the expiration of which the patient has suddenly died. With bilateral fluid, of medium amount, one pleura should be immediately evacuated. The removal of medium and small unilateral effusions is not immediately necessary and a short delay may promote repair or show spontaneous absorption. It is customary to wait two to three weeks, but earlier removal may well be considered. It alleviates symptoms from pressure and may prevent the formation of venous thrombi and the danger of pulmonary infarction. The withdrawal of fibrinous material, hindering absorption, may shorten the course. The danger of adhesions, permanent fixation of the lung in an abnormal position and persistent reaccumulation of fluid increases with the duration of the effusion.

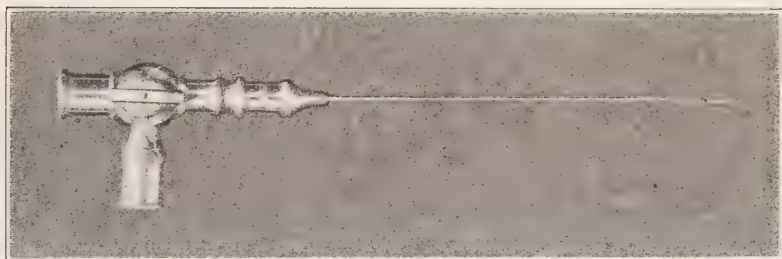
Selection of Cases for Tapping.—The character of the fluid is important in the decision between thoracentesis and thoracotomy. With clear fluid, thoracentesis is the operation of choice. Open incision is followed by suppuration, which is to be avoided. With turbid fluids the decision is more difficult. They are on the border line between sero-fibrinous and purulent effusion. Of 27 cases in the writer's series with turbid fluid containing an excess of polymorphonuclear cells, 15 were cured by thoracentesis alone. In 12, pus was found at later tapping and thoracotomy was performed. The tendency of pleural fluid to sediment within the chest must be remembered. A sample from the upper layer may be turbid, while pus may exist below. Turbid fluids secondary to lobar pneumonia or due to the pneumococcus are relatively favorable for thoracentesis. With merely an excess of polymorphonuclear cells in the differential count, tapping alone may be considered. Pneumococci may be found in such exudates, but are often incapable of cultivation. With abundant or necrotic leukocytes and pneumococci on cultivation, operation is usually necessary. Streptococcus infections are usually purulent, or rapidly become so, and generally demand operation. The general symptoms, the amount of fluid and rapidity of reaccumulation must also be considered.

Apparatus.—I have tried many different methods for the removal of pleural fluid and have abandoned more complicated equipment in favor of a nickeloid needle, three-way stopcock, and glass syringe which may be used both for diagnostic puncture and aspiration. The apparatus is shown in Fig. 13. One arm of the stopcock serves as a plunger to fit the aperture of the base of the needle, a second arm in line with the first receives the end of the glass syringe, while the third acts as a lateral outlet. The needle should be about 7 cm. long and of about 18-gauge. Syringes of 20-cc. capacity are convenient for diagnostic puncture and the aspiration of small amounts of fluid, but for removal of larger amounts more capacious syringes are desirable. When effusions of considerable

size are to be removed, it is well, in preparation, to sterilize at least two syringes of the capacity selected as fluid drawn by capillary attraction between piston and barrel tends after drying to obstruct the lumen. The stopcocks must be renewed after much use as they fail after a time to maintain an air-tight connection.

Technique.—The site chosen for puncture will vary with the amount and position of the effusion. The puncture is usually made in the seventh space between the scapular and posterior axillary lines. The choice of this situation has certain advantages, in that the patient is not disturbed by seeing the procedure and the needle will be nearer the lower level of the fluid. As the dome of the diaphragm rises normally as high as the fourth interspace in the nipple line, the sixth rib in the mid-axilla and the eighth rib in the scapular line, a lower level cannot safely be chosen. In fresh effusions, the lung, the heart, and the diaphragm are displaced away from the selected site, and there is little danger of their injury, but with chronic cases, with narrowing of the interspaces, contraction of the side and

FIG. 13



Needle and three-way stopcock for the aspiration of pleural fluid. The needle should be about 7 cm. long and about 18-gauge. It is convenient to have other sizes at hand. Detachment of the needle from the stopcock, during aspiration, may be prevented by soldering the two parts together.

elevation of the diaphragm, a higher level should be selected. A thickness of 2 to 4 cm. or more under ordinary conditions must be allowed for the thoracic wall. In fat subjects, or in the presence of a thick layer of fibrin, the needle may fail to find fluid even at this distance. The patient is best placed on the bed to avoid unnecessary exertion. The puncture may be made with the patient reclining on the affected side at the extreme edge of the bed. *Local anesthesia*, as for exploratory puncture (see p. 248), should precede the operation. The instrument is slowly and carefully introduced, perpendicularly to the surface, just above the rib, to avoid the intercostal artery. It is pushed in until from the lack of further resistance the operator may judge that the point has reached fluid.¹

Symptoms and Difficulties during Evacuation.—Faintness and vertigo are not uncommon, and are usually due to psychic disturbance. An

¹ It is convenient to know that at the level of junction of the third costal cartilage with the sternum (sixth dorsal vertebra), the distance from the skin to the bloodvessels at the root of the lung in an average adult male was found by Piersol (Musser: *Jour. Am. Med. Assn.*, 1907, 48, 24) to be 7 cm. in the mid-axillary line on the left side and at a greater depth in other regions of the same transverse section.

occasional slight cough is frequent toward the end of the evacuation. If severe, the operation should be stopped. Cough may be due to pleural irritation, to hyperemia, or œdema of the expanding lung. If it persists, morphine may be given. Blood may rarely be expectorated during evacuation. It may arise from the rupture of small bloodvessels in the lung, from congestion, or from puncture of the lung with the trocar, and when it occurs it is best to discontinue the operation. Pain is not common, but, if severe is a contraindication to continuance, as it may indicate undue tension on pleural adhesions. There may be a feeling of dyspnoea and general discomfort, perhaps cardiac in origin, and severe enough to warrant a halt in the operation.

The presence of firm tissue in the track of the instrument can usually be appreciated as a resistance against forward or lateral motion. Introduction elsewhere may be more successful. Finally, there may be no fluid, but negative punctures never positively exclude it. Interruption of the flow during evacuation may be due to fibrin, apposition of lung or diaphragm against the end of the needle, or equalization of pressure within and outside the chest. The last may happen even with considerable fluid remaining, provided the lung is firmly bound down in a retracted position.

Amount of Fluid to be Withdrawn.—This depends on the size of the effusion. Absorption may follow removal of very small quantities. The rare occurrence of serious symptoms, and even of death, following the evacuation of large amounts of fluid is a warning not to be safely disregarded. With large effusions, as much as 1500 cc. may be withdrawn, provided no unfavorable symptoms arise during the process. Much larger quantities are often removed without unfavorable result, and with very large effusions, as much as 2000 cc. may be evacuated. If danger is to be avoided, however, this amount should only rarely be reached and never exceeded. The remaining fluid will probably be absorbed; if not, the procedure can be repeated. The longer the effusion has lasted and the older the patient, the smaller the amount of fluid which can be safely withdrawn. More abundant adhesions and less elastic lung then increase the danger. In the presence of pulmonary tuberculosis, especial care should be exercised in the removal of fluid to avoid rupture of adhesions and artificial pneumothorax.

Duration of the Operation.—It is safer to evacuate fluid slowly. A half-hour may be consumed in the removal of 1500 cc. in order that neighboring structures may gradually readjust themselves.

Repetition of Tapping.—One tapping suffices in about 75 per cent. of the cases. In about 20 per cent. of the remaining cases there is no more fluid after the second operation. In some cases evacuation must be frequently repeated.

Dangers of Thoracentesis. There is some danger which is reduced to a minimum by the strictest asepsis, the slow withdrawal of only moderate amounts of fluid without forcible aspiration and a careful selection of cases. Unavoidable accidents are extremely rare. Patients are more often sacrificed by hesitation and delay than by its use. The danger of converting a serous into a purulent effusion appears to be insignificant.

In rare cases *pneumothorax* may be due to puncture of the lung or the rupture of adhesions, pulmonary cavities, or emphysematous blebs during expansion. It is not infrequently due to the entrance of air through an unguarded needle or trocar. It may also result from accidental inflation of the pleural sac with an aspirating pump, if the tubing is misapplied. Infection of the pleura may follow the admission of air.

Subcutaneous emphysema may occur if the lung is wounded and air enters the track of the needle. It may be local or involve the greater part of the body, and is more common after exploratory puncture. Extension of malignant growth or tubercle along the track of the needle occasionally occurs. The removal of pleural fluid may lead to the detachment of thrombi in the heart or intrathoracic vessels, with monoplegia or hemiplegia as a result. Delirium and hysterical and epileptic attacks have been observed. Urticaria has been noted after thoracentesis, and should always suggest echinococcus disease.

Albuminous expectoration is rare; Osler observed the condition twice in 195 cases. It occurred once in my series. The albuminous expectoration usually begins during or shortly after the withdrawal of fluid. Its appearance may be delayed, however, for as long as eighteen hours. It is accompanied by cough and often by dyspnoea, which varies much in intensity and may be extreme, with cyanosis and rapid, feeble pulse. Rales may be heard over the lung during the attack. Its duration and intensity are very variable. It may last for as long as forty-eight hours, and the patient may die of suffocation. The fluid may amount to as much as a quart in two hours, but smaller quantities are more common. The expectorated fluid is serous and contains a variable amount of blood, frothy mucus, and albumin. In most instances an excessive amount of fluid (more than 2000 cc.) has been removed. The condition has been ascribed to evacuation of pleural fluid by way of the bronchi. This may happen if the lung has been perforated during the puncture. Spontaneous rupture or filtration through the lung has been suggested. It is more probably due, however, to pulmonary congestion, with œdema, for which Riesman suggests the term "congestion by recoil." It may be conjectured that compression of the lung is followed by changes in its blood-vessels, and that in the congestion after reëxpansion there is a transudation of serum. Of 51 cases of albuminous expectoration which I have reviewed¹ 13 were fatal. A consideration of the postmortem reports on 14 in which death immediately followed the operation or occurred after an interval, suggests that pulmonary inelasticity from pleural adhesions or complicating cardiac, pulmonary or mediastinal disease is probably an important contributing factor.

Death, in rare instances, has followed even simple exploratory puncture. Capps and Lewis² have shown that irritation of an inflamed pleura often gives rise to a reflex of cardio-inhibitory or vasodilator type, with lowering of blood-pressure. The inflamed pleura appears to be especially susceptible, and the nervous shock thus induced in dogs may be fatal.

¹ Lord: *Boston Med. and Surg. Jour.*, 1909, **160**, 469.

² *Am. Jour. Med. Sci.*, 1907, **134**, 868.

Such experiments indicate the wisdom of avoiding any unnecessary play of the instrument against the inflamed pleura.

Artificial pneumothorax has occasionally been fatal. Sudden death during or after the evacuation of pleural fluid may be due to embolism. Thrombi in the pulmonary veins or the *venæ cavæ* are the most frequent source. Syncope and death may occasionally be due to cerebral anemia, from afflux of blood to the reëxpanded lung. Fatal hemoptysis has followed the wounding of vascular granulation tissue in the lung or of blood-vessels lining the walls or traversing the lumen of pulmonary cavities. Such vessels may be also ruptured during expansion of the lung. Perforation of the diaphragm has been followed by fatal peritonitis or hemorrhage from the spleen. Miliary tuberculosis may, in rare instances, arise from infected thrombi set free from pulmonary vessels by the evacuation of tuberculous fluid. If the lung is adherent, fatal hemorrhage from pleural vessels may follow forcible aspiration. Injury of an atheromatous intercostal artery has been followed by fatal bleeding.

Results of Thoracentesis.—Following removal of fluid, there is usually marked improvement in the breathing and cardiac action. The color is better and there may be an increase in the amount of urine. The heart returns to its normal position unless prevented by adhesions or marked indurative processes. The temperature may fall at once, but gradual defervescence is more frequent. The duration and intensity of the pleuritis appear to be lessened. Reëxpansion of the lung is more rapid, absorption of the remaining fluid takes place, and subsequently deformity with contraction of the side, narrowing of the intercostal spaces, and displacement of the diaphragm and heart are less frequent.

After-treatment.—The operation of thoracentesis affects the general management of the case very little. The desirable period of absolute rest in bed will depend on the underlying cause of the effusion. Patients with tuberculous effusions should be treated as for pulmonary tuberculosis.

Acute Purulent Pleuritis.—**Etiology.**—Certain differences between the etiology of this and other forms of pleuritis may be mentioned.

PRIMARY FORM.—The proportion of cases in which empyema is apparently primary is small compared with fibrinous and serofibrinous pleuritis. Of 252 cases with empyema in this series, 83 (32.9 per cent.) may be classed in this group, against 64 and 63 per cent., respectively, for the fibrinous and serofibrinous form. Primary empyema is said to be more common in children, but expectoration is often absent and an effusion may make the detection of a pulmonary process difficult or impossible. The primary form is likely to be tuberculous.

SECONDARY FORM.—As in other varieties of pleuritis, disease of the lung occupies first place and can be demonstrated in a larger proportion of cases, since the pulmonary lesions leading to suppuration in the pleural sac are more easily detected. Of 252 cases, 158 (62.6 per cent.) appeared to be pulmonary in origin, including 140 of pneumonia (136 lobar pneumonia, 4 bronchopneumonia), 15 of pulmonary tuberculosis and 3 of abscess or gangrene. Gangrene leads to putrid exudates. The disease may arise by extension from the abdomen, the pericardium, or the other

pleura; it may complicate the infectious diseases (influenza, typhoid fever, etc.) or suppurative lesions in any part of the body. It may be caused by trauma and may follow the serofibrinous form. In children empyema is, in general, more frequent than serofibrinous effusion. The younger the child, the more likely is the exudate to be pus. In adults, serofibrinous effusions are much more common.

1. *Pneumococcus*.—This appears to be the most frequent organism occurring as a pure infection. Of 137 cases, the pneumococcus was found in 54 (39.4 per cent.). It is the most common cause of metapneumonic effusions, but may also be found in primary empyema and shows a marked tendency to die out. It may be found in smears from the pus but cultures from the same fluid may be sterile. To this is probably due the relatively favorable course of pneumococcus empyema. The type of pneumococcus in metapneumonic empyema is almost always the same as that found in the sputum. Precipitation tests for identification of type may be done directly on the chest fluid.

2. *Streptococcus*.—This was present in 28 (20.4 per cent.). Serofibrinous effusions containing streptococci are likely to become purulent. The organism is in most instances the streptococcus hemolyticus, less often the streptococcus viridans.

3. *Tubercle Bacillus*.—This has not been shown to be as frequent a cause of purulent as of serofibrinous effusions. Of Netter's 109 cases, 12 were found to be tuberculous. Of 310 cases of empyema in Hedblom's¹ series 29 (9.35 per cent.) were proved to be tuberculous. The finding of other organisms does not exclude the tubercle bacillus nor does the presence of the tubercle bacillus alone exclude other organisms such as the pneumococcus, which may have died out.

4. *Staphylococcus*.—This is relatively infrequent, occurring in only 5 (3.6 per cent.).

5. *Mixed Infections, etc.*—Infection with more than one organism was found in 22 (16 per cent.). The pus was sterile in 25 cases (18.2 per cent.), and infection with the tubercle bacillus or the pneumococcus may be suspected. Other organisms than those already mentioned are uncommon. Influenza bacilli, typhoid bacilli, *Bacillus mucosus capsulatus*, *Streptococcus capsulatus*, diphtheria bacillus, colon bacillus, actinomyces, etc., have been found. Mixed infections are usually present with putrid exudates.

Types of Disease.—The purulent pleurisies have been separated into different groups according to their bacterial etiology. Mixed infections with two or more organisms are common, and the tubercle bacillus may coexist, but elude detection. Sterile exudates are difficult to place; they are usually due to the tubercle bacillus, rarely to the pneumococcus. As yet no distinctive clinical picture can be formulated for the various forms.

Pathology.—The pleura is the site of a fibrinous or fibrino-purulent layer. It is grayish-white or yellowish, and may be greatly thickened. The inflammation may be general or circumscribed. The sacculation of

¹ *Jour. Am. Med. Assn.*, 1923, **81**, 999.

fluid is not infrequent. Erosion, ulceration, or even perforation of the visceral or parietal pleura may be found. These destructive processes may be single but are more commonly multiple and limited to the pulmonary layer. After long-standing empyema, calcification and the formation of bony plates may take place in rare instances.

In fatal cases other organs are seldom uninvolved. The lung is the most frequent site of changes, from which the pleural disease has usually arisen secondarily. Lobar pneumonia, bronchopneumonia, abscess, and gangrene may be the source of the process. After long-standing empyema, chronic interstitial changes may occur about the lung and penetrate the pulmonary tissue along the interlobar septa, the so-called pleurogenous interstitial pneumonia. Suppurative pulmonary lesions and bronchiectasis are likely to coexist. It is often difficult to tell whether the lung is primarily or secondarily invaded. In some instances, pleural suppuration extends to the pericardium, peritoneum, or the mediastinum, from which the opposite pleura may become infected. Endocarditis is not uncommon. The spleen may be large and soft. Thrombosis of intrathoracic or other vessels may be present. Cerebral abscesses may occur. Tuberculosis of the pleura, lungs, or bronchial glands was present in 9 of 38 cases at autopsy. Tuberculous lesions in more remote parts of the body were found in 2. Thus, about 30 per cent. showed tuberculosis in some part of the body.

Location.—Of 248 cases, the right side was affected in 122, the left in 121, and both in 5. Purulent are more often encapsulated than serofibrinous fluids. Encapsulation was discovered in 8 cases. When empyema complicates pneumonia, the effusion is usually at the base irrespective of the site of the pneumonic process.

The Effusion—No sharp dividing line can be drawn in gross appearance between serofibrinous and purulent fluids. The effusion may be serofibrinous at first and become purulent later. There is often, however, an excess of polymorphonuclear cells in such fluids from the beginning. The fluids may be yellowish, greenish, reddish or even frankly red, brownish or chocolate-colored from the presence of blood. With large amounts of pus they are grayish, greenish-yellow, or cream colored. They may be without odor, sweetish, or fetid. In gangrene of the lung or pleura they often have a horribly offensive odor. The specific gravity is higher than in serofibrinous fluids and may reach 1030 or more.

Symptoms.—These are usually the same as in the serofibrinous form and only certain differences need be mentioned. They are not distinctive of empyema. The onset is likely to be more acute. An insidious onset and latent course are less common than in the serofibrinous form. Toxic symptoms are more common and more severe. In general, the temperature is higher; of 145 cases only 2 ran an afebrile course. From 101° to 103° F. is an average pyrexia, but the temperature reaches 104°, 105° F., or even higher in a larger proportion of cases, with wider variation between the morning and evening elevations. The respiration and pulse are likely to be more rapid. Recurring chilliness or chills, more rapid loss of strength and weight and increasing pallor may be mentioned. Between the various infections there are no constant differences. *Pneumococcus empyema*

may be relatively mild. Streptococcus infections are more severe and putrid exudates are accompanied by most marked disturbances. In the latter, bad taste in the mouth, foul breath, and foul sputum may be present. Uncomplicated tuberculous effusions may run an afebrile and long course without marked general symptoms. In rare instances empyema may persist without symptoms for months or years. In Faisans and Audistère's case the disease may have lasted for forty years. At autopsy there was sterile fluid contained in a space, the walls of which were transformed into cartilaginous and osseous tissue.

Physical Signs.—These are such as have been considered under Serofibrinous Effusion. The affected side may be more prominent, with wider intercostal spaces which may actually bulge. Edema of the chest wall is uncommon, but more frequent with purulent than with serous fluid. The subcutaneous veins may be dilated. A disproportion between the amount of fluid and the severity of the symptoms may be suggestive. In children the breath sounds may be loud and bronchial over a purulent effusion. The axillary glands are occasionally enlarged on the affected side. The spleen may be enlarged. In long-standing cases, especially in children, clubbing of the fingers may occur.

Pulsating Empyema.—This is more commonly associated with supuration in or about the pleural sac. Of 95 cases analyzed by Sailer¹ there was pus in the pleural sac in 71, and of these there was tumor (empyema necessitatis) in 38. In 13 there was intrapleural or extrapleural abscess. The remaining cases were non-purulent or their condition was not definitely known. The condition appears to be more common in males and in early life. Pulsations may be diffuse or localized, single or multiple, and are more often on the left side. They are most common in the parasternal regions, but may occur in the lower lateral and posterior parts of the chest. Pulsation is probably due to an accumulation under pressure of fluid which is apposed to a lung made inelastic by collapse or pathological changes, and to some local or general weakness of the thoracic wall.

The Blood.—*White Cells.*—In 28 cases of primary empyema the white count was above 12,000 in all but 6. The 6 cases with a low white count recovered after operation. The white count may be of value in distinguishing uncomplicated tuberculous serofibrinous effusion from empyema, only 3 of 33 cases with the former showing a white count above 12,000.

Complications.—These are much as in serofibrinous pleuritis.

1. *Extension to Neighboring Organs.*—This is more common in empyema. (a) *Perforation of the Lung.*—This may be *latent* and indicated only by the expectoration of muco-purulent sputum. Evacuation of small amounts of pleural pus by this means is frequent. The complication is frequently overlooked and pneumothorax only rarely occurs. In other cases the perforation is *obvious*. In this form pneumothorax is more common, but does not necessarily occur. There is a sudden paroxysm of cough, with the evacuation of a large amount of pus. If perforation occurs while the patient is asleep or if the lung is suddenly

¹ *Am. Jour. Med. Sci.*, 1904, 128, 225.

flooded, death may result from suffocation. Single or multiple fistulous tracts may connect the pleura with the bronchi and pneumothorax may thus arise. Invasion of the lung usually leads to multiple abscesses connecting with the bronchi. In some instances the affected lung presents a honeycombed appearance. Single pulmonary abscesses are less common. It is difficult to tell in individual cases at autopsy whether the lung has been primarily or secondarily involved. Of 11 cases with pulmonary suppuration and empyema at autopsy, abscesses were multiple in 8, single in 3. Pulmonary gangrene may occur, but is less common. Chronic interstitial pulmonary changes are likely to follow if the patient recovers. Of 145 cases, obvious perforation occurred in 5. One patient recovered. A second had persistent cough, with abundant purulent sputum and frequent attacks of hemoptysis, but was otherwise well six years after operation. The 3 remaining patients died, 1 from suffocation, the others from sepsis. Evacuation by the lung does not obviate the necessity of operation, which should be done to spare the lung further damage. Pulmonary perforation may occur at any time, but is uncommon before the third or fourth week.

(b) *Perforation of the Thoracic Wall (Empyema Necessitatis).*—This is less common than pulmonary perforation but more favorable and may be followed by complete evacuation and recovery. The abscess may point in any part of the chest, but more often in the parasternal region or in the fifth interspace outside the nipple line, the thinnest regions of the chest. The perforation may be single or multiple. It seldom occurs before the end of the first month, but may take place at any time after this period. The abscess usually forms an irreducible fluctuating tumor, becoming more tense with forced expiration or cough. It is dull or flat on percussion. The opening into the thorax may be at some distance from the site of the tumor, the rupture of which may be followed by discharge of a large amount of fluid. Forced expiration and cough may hasten, inspiration may diminish the flow. The tumor may pulsate. Evacuation by spontaneous perforation is usually incomplete. The fistula is likely to close and the pleural pus to reaccumulate, with subsequent perforation in the same or other places. Cure by this means is rare and operation is indicated. Caries of the ribs and necrosis of the soft parts may arise from the perforation. Erosion of an intercostal artery may lead to fatal hemorrhage. Perforation is more common in streptococcus, tuberculous, mixed, or putrid infections. Actinomycosis should always be considered with abscesses of the chest wall arising by extension from within. Simple thoracic abscesses may be unaccompanied by pulmonary or pleural changes and are uninfluenced by changes in intrathoracic pressure. The distinction may be impossible before exploration by operation. Suppuration in the tissue between costal pleura and thoracic wall (peripleuritis) leading to external perforation may simulate encapsulated empyema necessitatis.

(c) *Perforation of the Diaphragm.*—This is more serious and may lead to local or general peritonitis. It is often difficult in individual cases to tell whether the infection has spread from the pleura to peritoneum or in the opposite direction. Obvious gross lesion may be absent. In other

cases the site of the perforation may be readily found. Peritonitis was present in 9 of 38 autopsies on cases of empyema in my series. It was general in 7, localized in 2. In one case an encapsulated diaphragmatic empyema pointed in the right hypochondrium; recovery followed operation. An abdominal abscess, starting from the pleura, may perforate the stomach, the intestines or the kidney. It may extend along the spine to the iliac fossa and simulate psoas or lumbar abscess.

(d) *The œsophagus may be perforated* with the formation of pleuro-œsophageal fistulæ.

(e) *Infection of the pericardium* is probably more often present than statistics show. It was recognized during life in 4 of 145 cases, but was present at autopsy in 6 of 38 cases. Inflammation may also extend to the mediastinum.

2. *Metastatic Lesions.*—It is uncertain in individual cases whether suppurative lesions in remote parts of the body are primary or secondary. They may arise by extension of the pleural infection to the intrathoracic veins or the endocardium. Cerebral abscesses are among the most dangerous complications, and are usually multiple, as in 3 of 38 autopsies in my series. Pulmonary abscesses were associated in 2. In 1 the cerebral abscesses were unaccompanied by suppurative foci elsewhere than in the pleura. Septicemia is common in empyema.

3. *Amyloid degeneration* may complicate long-continued suppuration.

Causes of Death.—The same danger of sudden death from similar causes obtain in purulent as in serofibrinous effusion. It is uncommon in fatal cases not to find suppurative processes in neighboring or other parts of the body. Peritonitis is one of the most frequent of coincident infections, and was present in 9 of 38 fatal cases, but the complicated character of fatal cases makes it difficult to judge between principal and contributing causes. Pneumonia, pulmonary abscess and gangrene, pericarditis, endocarditis, thrombosis of intrathoracic veins or the auricles, with or without infarction, cerebral abscesses and meningitis may be regarded as important factors, either singly or combined. The streptococcus is the most frequent organism, but pneumococci are often present and other organisms may be found.

Relapse.—Recurrence of empyema in the same place after complete recovery does not occur, because of the almost constant obliteration of the pleural sac. Incomplete absorption or removal may, however, be followed by a return of symptoms and an increase in the amount of fluid. Incomplete evacuation, insufficient drainage, encapsulation, the presence of undiscovered pockets of pus or the development of empyema elsewhere may be responsible for a second accumulation of fluid. Pitt¹ reported the unusual postmortem finding of a smooth pleural surface without adhesions in a child who had empyema one year before.

Sequelæ.—It is rare not to find signs of the previous disease in patients who have recovered from empyema. There is diminished expansion of the affected side, which often looks smaller, and measurement shows that it is contracted. The interspaces are relatively narrow. Toward the

¹ *Brit. Med. Jour.*, 1908, ii, 1075.

base is slight relative dullness, its upper limit often highest behind and extending in a nearly horizontal line toward the axilla, where it gradually descends to the inferior pulmonary margin in the antero-lateral thoracic region. The extent of dullness is variable and may involve half the chest. The tactile fremitus may be diminished over the dull area. The breathing, voice sounds and whisper may be diminished, but are often unchanged. In cases with a long course before evacuation takes place, with abundant connective-tissue formation about the lung or within its substance, the lung may be partially or wholly incapable of reëxpansion. A space is left which is filled by fibrous tissue, by the collapse of the chest wall, dislocation of the mediastinum and heart toward the affected side, displacement upward of the diaphragm and partial expansion of the lung, depending on the changes which have taken place in and about it. In rare cases, with dullness, there may be signs suggestive of slight degrees of pulmonary solidification. These may be due to interstitial changes in the lung, or, if marked retraction has taken place, to proximity of the larger bronchi to the chest wall. In the young, with less resistant thoracic walls, marked deformity with retraction of the side, drooping of the shoulder and lateral deviation of the spine may result.

Pain of variable and usually slight intensity may persist in the affected side. Of 26 patients investigated on this point, 8 still had pain for periods of one to seven years after discharge.

Diagnosis.—Inasmuch as the treatment of empyema due to the tubercle bacillus differs from that in other types of the disease the physician is under obligation to establish or exclude tuberculosis as the cause by every possible means. The primary form and empyema secondary to pulmonary or other tuberculous processes are likely to be tuberculous. Examination of the pus affords valuable evidence as to the nature of the underlying process. The diseases with which pleural effusion may be confused, the differentiation of pleural fluids of different character, the method of employing exploratory puncture and the examination of pleural fluids have been discussed under Serofibrinous Pleuritis. Certain additional features in the diagnosis of empyema may be emphasized with special reference to exploratory puncture, exploratory incision, and the examination of purulent fluid.

Exploratory Puncture.—This is indicated if pus is suspected. By hesitation and delay, the disease may be converted into a chronic and incurable affection. In acute cases, with typical signs of fluid, it is practically devoid of danger, and, if present, pus can usually be demonstrated by this means. In some cases, however, it is missed by the needle or is too viscid to flow. A negative puncture does not exclude pus.

Cases in Which Exploratory Puncture is Dangerous.—In cases of empyema of long standing, in which there is contraction of the side, elevation of the diaphragm, and secondary, suppurative lesions in the lung, or in cases in which empyema complicates pulmonary abscess, gangrene, bronchiectasis and interstitial pneumonia, the conditions are less favorable for exploratory puncture. The pleural pus is often small in amount and may be encapsulated between lung and diaphragm or in other parts of the chest. It is well to confirm the results of physical examination by

radioscopy. Exploratory puncture is not without danger in cases thus complicated. Bloodvessels lining the walls or traversing the lumen of pulmonary cavities or fresh granulation tissue, injured by the needle, have been the source of fatal hemorrhage. Perforation of the elevated diaphragm has caused fatal peritonitis. In such cases, in which from the history, the physical signs, and the roentgen-ray examination there is good reason to suspect pus, the demonstration of which by puncture has failed or cannot be safely undertaken, it is better to resort to exploratory incision.

Exploratory Incision.—This is indicated when there is good reason to suspect pus which cannot be demonstrated by exploratory puncture or in complicated cases in which it is a less dangerous procedure. It should be entrusted only to an experienced surgeon, and undertaken only in cases in which from the history, physical, roentgen-ray and sputum examination there is little or no ground for the belief that the suspected empyema is of tuberculous origin. The chief danger is artificial pneumothorax, which may arise if the lung is free. Incision and costatectomy, with care not to wound the pleura, will disclose the condition of the underlying tissue.

Examination of Pleural Pus.—Operation should not be undertaken until the fluid obtained by exploratory puncture has been examined. Clear or cloudy serofibrinous effusions should be examined as already indicated. Cultures should always be made regardless of the gross appearance of the fluid. With frank pus, smears should be stained for tubercle bacilli and other organisms. If the smear shows no organisms and cultures are sterile the empyema is probably tuberculous. Tubercle bacilli may be demonstrated in stained smears or by animal inoculation. Animals cannot be inoculated with large amounts of pus or intraperitoneally without danger of loss of the animal before the development of tuberculous lesions. It is best therefore to inject only 1 to 2 cc. of pus under the skin. In patients operated on, the diagnosis of tuberculosis may be made by microscopic examination of stained sections of a small piece of excised pleura.

Prognosis.—Absorption of empyema rarely occurs. Spontaneous disappearance of pus has been noted in isolated cases and may be due to latent perforation of the bronchi. Recovery may follow obvious perforation of the lung, but usually with distressing and dangerous complications. After perforation of the chest wall recovery may follow. Most cases, if untreated, end in death. Of 252 cases in my series 56 (22.2 per cent.) died in hospital.

Treatment.—In general, pleural pus should be evacuated as soon as the diagnosis is made. *Constant, free drainage is essential for prompt and permanent cure.*

1. **THORACOTOMY WITH COSTATECTOMY.**—This is the operation of choice, for chronic and encapsulated empyema, when the empyema cavity is walled off by adhesions of sufficient firmness to prevent lung collapse on opening the thorax. It should be avoided and the pus evacuated by other means (see below) in fresh empyema. Many lives may be saved by a more conservative procedure early and resort if necessary later to the

more radical operation. It is probably best to wait until the effusion has changed from serofibrinous to purulent or let an interval of about two weeks elapse from the time of onset to the resort to radical operation. The incision is best made in a dependent part of the pleural cavity, with resection of the seventh or eighth rib in the posterior axillary line. Pus should be evacuated slowly. Irrigation of the cavity with an antiseptic solution, as in the Carrel-Dakin technique, hastens recovery. With empyema necessitatis, enlargement of the perforation in the chest wall may suffice if this is in a favorable position for drainage. Otherwise, a second opening in a more suitable position should be made. If the pus is encapsulated, the incision must be made where drainage will be most effective. Thoracotomy alone may afford insufficient drainage and costatectomy is often necessary later.

2. OTHER METHODS.—These are less efficient since drainage is often neither constant nor free, but they may be used in selected cases, as a preliminary to the radical operation or as palliative procedures.

(a) *Thoracentesis*.—This may be considered for effusions on the border line between the serofibrinous and purulent forms. It is indicated for the evacuation of an exudate of large size, with or without pressure symptoms, as a life-saving measure or a preliminary to operation, thus avoiding the danger of more rapid evacuation, and as a palliative procedure in empyema complicating advanced pulmonary tuberculosis. Evacuation by puncture, not open incision, is also indicated in sterile exudates or those containing tubercle bacilli without other organisms. Although repeated puncture has been advised for pneumococcus empyema, especially in children, it is uncertain, likely to be followed by reaccumulation, and leads to complications and greater deformity of the chest. It frequently delays operation, often necessary later, and subjects the patient to an unjustifiable risk.

(b) *Closed Suction Method*.—This is a modification of Bulau's siphon drainage in which a rubber catheter was passed through a trocar, armed with a stopcock, and the trocar withdrawn. One end of a short piece of glass tubing was inserted into the free end of the catheter and the other into a rubber tube leading to a receptacle attached to the bed or placed on the floor. Whittemore¹ keeps the catheter closed by clamping it with hemostatic forceps and fastens it in place by adhesive plaster and suture to the chest wall. With large purulent effusions 3 to 4 ounces are removed every twenty minutes by suction with a 4-ounce glass syringe until the cavity is dry. The cavity is irrigated with normal saline every two hours for the first twenty-four hours and thereafter with Dakin's solution. Daily irrigation with salt solution helps to prevent clogging of the catheter. Infection of the skin about the catheter may be prevented by painting with tincture of iodine once daily after the third day.

The method has the advantage of slow evacuation, avoidance of a large operation wound and, still more important, largely eliminates the danger of open pneumothorax. It has the disadvantage that the apparatus requires constant attention, pus is less likely to be completely

¹ *Boston Med. and Surg. Jour.*, 1922, **187**, 16.

evacuated and masses of fibrin may readily obstruct the catheter. The absence of adhesions in acute cases and consequent danger of lung collapse if costatectomy is performed make this the operation of choice in such cases, at least as a temporary expedient. The method may also be used in patients at the extremes of age, in those whose general condition is such that a radical operation is dangerous, in relatively benign pneumococcus empyema without much fibrin and in double empyema in which pneumothorax is especially to be feared.

Tuberculous Empyema.—If the exudate is sterile or contains tubercle bacilli alone, surgery is in general contraindicated and removal should be accomplished by aspiration. If the fluid reaccumulates, aspiration should be repeated. Thoracotomy and costatectomy lead to secondary infection and the formation of a persistent sinus. In tuberculous cases in which a bronchial fistula is impending or established, however, constant free evacuation is desirable for the purpose of sparing the lung and it is then justifiable to drain the abscess, preferably by the closed-suction method, but if necessary by thoracotomy and costatectomy. If the tuberculous empyema also contains pyogenic cocci, thoracentesis alone cannot be expected to provide adequate evacuation to avoid the dangers of general infection and more radical measures are indicated. In acute cases without sufficiently firm adhesions to prevent lung collapse, closed-suction aspiration is the procedure of choice. In more chronic tuberculous empyema with mixed infection thoracotomy and costatectomy may be done. In general, tuberculous empyema is the most unfavorable form. Of 12 patients, with sterile exudates, only 1 of whom showed tubercle bacilli in the sputum, 3 died in hospital. Of the remaining 9 patients, 6 have been traced. All have died except 1, who had a discharging sinus, seven years after operation, but was otherwise well. Sterile exudates are usually, but not necessarily, tuberculous.

Anesthesia.—Local is to be preferred to general anesthesia for empyema operations. Blocking the intercostal nerves is usually sufficient for siphon drainage and paravertebral anesthesia for costatectomy. If general anesthesia must be used, gas-oxygen is less dangerous than ether. Aside from the undesirability of general narcosis in the presence of respiratory infection, there is special danger with empyema that the bronchial tubes may be flooded with pus by rupture of the pleural cavity into the lung while the patient is unconscious.

After-treatment.—Expansion of the lung may be favored by various devices, permitting the outflow of pus and air through the drainage tubes during expiration, but preventing the reëntry of air during inspiration. A thin layer of impervious material (mackintosh, protective silk) may be applied over the opening of the tubes. The dressing itself, when soaked with secretion, may suffice. In favorable cases the sinus usually closes within two months. After closure of the sinus, respiratory exercises are valuable. Throughout the illness, every means should be taken to build up the general health.

Delayed Healing.—Failure of the abscess to heal may be due to the formation of dense fibrous adhesions about the cavity from delay in

the performance of the operation. It may also, as Eggers¹ suggests, be due to too early open drainage and permanent fixation of the lung in a collapsed state. Of other causes, inadequate drainage, bronchial fistulæ, tuberculosis of the pleura and foreign bodies such as bismuth paste, fragments of necrosed ribs, sections of rubber tubing, safety pins, etc., may be mentioned. Osteomyelitis of a rib may prevent closure of the sinus.

Results of Operation.—The mortality of the operation itself is very low. Even in the most desperate cases evacuation by some means is justifiable.

Diaphragmatic Pleurisy.—Pleuritis may be limited to the diaphragmatic region. It may be partial or general, fibrinous, serofibrinous, or purulent. Large collections of fluid are rare. Owing to its inaccessible site, physical signs are often lacking and the diagnosis may rest on symptoms and roentgen-ray findings alone. The pain may present features already described under fibrinous pleuritis, but is more likely to be referred to the lower thoracic or abdominal region. This may be due to implication of the lower intercostal nerves which supply the skin and muscles of the abdominal wall, as well as the parietal and diaphragmatic pleura. In the writer's series, abdominal pain was noted in 5 of 82 cases with primary fibrinous, in 5 of 374 cases with primary serofibrinous, and in 2 of 33 cases of primary purulent pleuritis. It may be associated with muscular spasm and tenderness, and the picture may simulate an acute abdominal affection for which laparotomy has been performed. Capps² has shown that when the central portion of the diaphragm is irritated pain is referred to the regions supplied by the third and fourth cervical nerves, from which part of the phrenic nerve takes its origin. In a series of 93 cases a diaphragmatic pleurisy referred neck pain was present in 62, or a little over two-thirds.³ It was usually located along the trapezius ridge, occasionally over the shoulder cap and in the supraclavicular space. Pressure over the hyperalgesic area was often painful. Kelly and Weiss⁴ found tenderness over the twelfth rib posteriorly in 17 of 22 cases of diaphragmatic pleurisy. Capps and Coleman⁵ have shown that irritation of the central portion of the diaphragmatic peritoneum produces pain in the region of the trapezius ridge, while irritation of its outer margins causes pain over the lower costal region and subcostal abdominal wall. The breathing may be partially or wholly thoracic in type and the diaphragm phenomenon absent on one or both sides of the chest. Dyspnoea may be marked and attacks simulating angina may be observed (Andral). Obstinate singultus may occur. The phrenic and pharyngeal branches of the vagus are implicated and probably through irritation of the former in the diaphragm. The swallowing of food may cause pain. Roentgen-ray examination is likely to show some abnormal modification in the contour of the shadow of the diaphragm in the presence of diaphragmatic pleurisy.

¹ *Jour. Am. Med. Assn.*, 1920, **75**, 995.

² *Arch. Int. Med.*, 1911, **8**, 717.

³ Capps: *Oxford Med.*, vol. **2**, 174.

⁴ *Am. Jour. Med. Sci.*, 1918, **156**, 808.

⁵ *Arch. Int. Med.*, 1922, **30**, 778.

Encysted Empyema.—Encapsulation of uncomplicated transudates does not occur. It is rare with serofibrinous fluid, but more common with pus. In occasional instances fluid may be serous in one and purulent in another pocket. Sacculation was discovered in only 1 of 1085 cases of serofibrinous effusion, but in 8 (3.2 per cent.) of 248 empyemas in this series. It is, however, probably much more common than these figures show, for in 38 autopsies on patients with empyema it was noted in 12 (31.5 per cent.). Sacculation is more likely to occur in small or medium effusions and in those in which the fluid is at a standstill. Encapsulation may occur between (1) diaphragm and lung, (2) the lung and chest wall, and (3) the lobes of the lung.

(a) **Encapsulation of Pus Between Diaphragm and Lung** is more common than in other situations. In most instances the empyema is at first free, but is *later* walled off by adhesion of inflamed and apposed pleural surfaces in the posterior and inferior thoracic region. This was noted in 5 autopsies in the present series. Sacculation of fluid above the diaphragm without apposition to the thoracic wall may occur. The effusion may be bounded by lung and diaphragm, or by lung, diaphragm and the mediastinum. Perforation of lung or diaphragm may be the first objective sign. The symptoms may suggest diaphragmatic pleurisy. The heart and the organs below the diaphragm may be dislocated, expansion of the affected side may be deficient, and an area of dullness several inches above the base of the lung may be discovered where diminished breathing, voice sounds, and tactile fremitus may be suggestive. Pleuritic friction may occur. If, as is often the case, more extensive pleuritis has preceded the sacculation, the physical signs may be difficult of interpretation.

(b) **Sacculation Between Lung and Chest Wall.**—This is not uncommon and is likely to occur in cases in which a previous pleuritis has obliterated the diaphragmatic portion of the pleural sac. It may occur in empyema in which, following operation, the sinus has been allowed to close too quickly. Such encapsulation is more common over the base, but may be observed over other parts of the lung.

(c) **Interlobar Empyema.**—Inflammation of the interlobar pleura occurs as part of a general pleuritis. An effusion of fluid may be limited externally by the thoracic wall, internally by the lobes of the lung between which it lies. In rare instances the effusion may not extend to the chest wall, and is bounded on all sides by the lung. The symptoms are not distinctive and the diagnosis is difficult. The localization of the process in the region of the interlobar septa and the absence of signs above and below this region are most likely to suggest the diagnosis. Examination by the roentgen-rays may be of great assistance. Sacchonaghi¹ has reviewed the literature.

Diagnosis.—Laennec regarded egophony as an important sign. Localized tenderness may be elicited by firm and deep pressure in the interspaces. Sacculated and especially interlobar empyema is likely to be confused with pulmonary abscess. The gross character of the sputum

¹ *Gesamt. geb. d. prakt. Med.*, 1910, 10, 151.

may be suggestive. The sudden expectoration of a large amount of homogeneous pus, little mixed with mucus, may suggest empyema. The discovery in the expectoration of elastic tissue with an alveolar arrangement is diagnostic of pulmonary abscess, but does not exclude a complicating empyema. Tumors of the lung must also be considered. Exploratory puncture is usually recommended for diagnosis, but its danger has been noted and exploratory incision may be safer.

Treatment.—Perforation of the lung has been followed by spontaneous recovery. If perforation has already occurred when the patient comes under observation, the decision between an expectant policy and operation must be made on the exigencies of the individual case. If the empyema can be reached, its evacuation is indicated.

Eosinophilic Pleural Effusion.—The presence of pleural effusion containing eosinophiles in considerable numbers has been reported by several observers and Schwarts¹ found 68 cases in a review of the literature. A number of instances, collected by Clarke² have since been reported. The pleural eosinophilia has been noted in traumatic hemothorax, in pleurisy with effusion in connection with tuberculosis, typhoid fever, pneumonia, polyarthritis and other infections, pulmonary infarction and malignant disease. An eosinophilia in the circulating blood may accompany the pleural eosinophilia. The cause is unknown and the condition appears to have no diagnostic significance.

Actinomycosis and Streptothricosis of the Pleura.—Two kinds of parasites must be recognized, *i. e.*, *Actinomyces bovis* and *Streptothrix*. Although the two parasites present well-marked biological differences, the clinical and pathological picture is, in general quite similar.

Actinomycosis.—In a large proportion of the cases this arises by extension from the lung. Pleural invasion may also occur from the œsophagus, by extension downward from the neck to the mediastinum and thence into the pleura, or from abdominal lesions which perforate the diaphragm. Metastasis is a possible mode of origin. The pleura overlying the involved tissue is the site of a fibrinous exudate. If adhesion of the visceral and parietal layers does not take place, a serofibrinous effusion or, more commonly, an empyema may result. The manifestations on the part of the pleura may mask the primary focus of the disease. Perforation of the chest wall is a characteristic feature and may take place at any part of the thorax, but is more common in the lower thoracic region. Erosion of the ribs may occur.

There is no distinctive clinical picture. Actinomycosis should be suspected in empyema, especially when associated with chronic pulmonary suppuration, interstitial pneumonia, abscess, gangrene or empyema necessitatis. The diagnosis can be made only by finding granules with branching, Gram-staining filaments and radially disposed club shaped, eosin-staining peripheral bodies. The prognosis is very unfavorable. A few arrested or apparently cured cases have been reported. The treatment is surgical, combined with the internal administration of large doses of iodide of potassium.

¹ *Ergebn. d. allg. Path. u. path. Anat.*, 1914, **17**, 138.

² *Jour. Am. Med. Assn.*, 1922, **79**, 1591.

Streptothricosis.—This appears to be much less common. Infection of the pleura takes place by extension from the lung. The changes are similar to those in actinomycosis, and may closely resemble tuberculosis. The diagnosis is made by finding thread-like, branching organisms, which, in most cases, resist decolorization with weak acids and alcohol, but are less "acid-fast" than the tubercle bacillus, do not form granules or masses of closely packed interlacing filaments with the characteristic "clubs" at the periphery and are much more readily cultivated than either tubercle bacilli or actinomyces.

Peripleuritis.—Secondary inflammation of the peripleural tissue is associated with all pleural and many parapleural infections. A primary form has been described, in which, independent of neighboring disease, there is inflammation and suppuration of the tissue between the costal pleura and the chest wall. Idiopathic peripleuritis is rare. It is usually localized and may be acute or chronic. Extension inward is uncommon; perforation of the chest wall is frequent. There are the usual symptoms of suppuration. Movement of the affected side may be restricted. The tissue overlying the inflamed area is swollen. The involved region is dull, the breathing and fremitus diminished or absent. Fluctuation may be established. The diagnosis may be impossible before operation, and even then it may be difficult to distinguish between an encysted empyema and a peripleural abscess. The absence of signs of disease at the base of the chest, slight or failing dislocation of the heart and the lack of shifting dullness may distinguish between peripleural abscess and ordinary empyema. The prognosis has been regarded as unfavorable. Early diagnosis followed by prompt surgical treatment may be expected to give favorable results in simple (non-tuberculous) and uncomplicated cases.

Syphilis of the Pleura.—Cases of pleurisy with a positive Wassermann test on the blood and pleural fluid have been reported. In some instances negative inoculation tests in animals have failed to show tuberculosis in such cases, but the syphilitic character of a pleurisy has not been established.

Chronic Pleuritis.—1. **Dry Pleurisy.**—This occurs as a sequel to fibrinous, serofibrinous or purulent pleuritis. Even in the mildest cases of fibrinous pleuritis the pleura rarely escapes some damage. The pleura overlying a pulmonary process may be merely thickened. Adhesions between the pulmonary and parietal layers are common. The pleura may reach a centimeter or more in thickness and enclose single or multiple pockets of serous or purulent fluid. Deposition of lime-salts may have taken place. The neighboring lung is often contracted and fibrous. Bronchiectasis or abscess is frequent. The interstitial pulmonary changes may be due to extension from the pleura, but it is difficult to exclude their independent origin. The pleural changes may be simple or tuberculous. In the latter instance, small tubercles, fibrocaseous or calcified areas may be found in the indurated tissue. The site is usually at the bases, when it follows pleurisy with effusion. In tuberculous cases it is frequently at the apices, and extensive pleural thickening may complicate slight pulmonary infections.

There may be no symptoms. Pain of varying and usually slight intensity may be present. Pleuritic friction may exist without subjective symptoms. Adhesions usually prevent the rubbing of the two pleuræ together. Chronic apical pleuritis may give rise to depression of the supra- and infraclavicular fossæ, to contraction of the apex, dulness, diminished breathing, voice sounds, and tactile fremitus, but coexistent pulmonary lesions may make the signs of thick pleura atypical. An apical process is tuberculous in a large proportion of the cases. In non-tuberculous cases, with retraction of the side and fixation of the lung, pulmonary gymnastics may be prescribed to favor expansion and improve the breathing capacity.

2. Pleurisy with Effusion.—In rare instances serofibrinous or purulent fluid continues to reaccumulate after repeated thoracentesis or operation.

(a) *Serofibrinous Form.*—Persistent reaccumulation may be due to failure of the retracted and adherent lung to expand and a neglect of early tapping may be responsible. In the absence of malignant disease and obvious pulmonary tuberculosis, a resort to operation may be considered after other measures have been tried. It should be advised with caution, however, for it necessarily induces empyema, which may also fail to heal, if the lung is adherent.

(b) *Empyema.*—In this, too early open drainage with resulting lung collapse and fixation of the lung in a collapsed state, undue delay in securing drainage with consequent induration of the walls of the cavity, inadequate drainage, persistence of undrained pockets, the presence of bronchial fistulæ, foreign bodies in the cavity and tuberculosis as a cause may be concerned in failure of the empyema to heal. Simple costatectomy with or without irrigation with Dakin's solution may be sufficient to promote healing. Exploration may lead to rupture of undrained pockets into the field of operation or the removal of foreign bodies. Bronchial fistulæ may eventually heal after adequate drainage is established. If not, more radical measures may be necessary. In cases in which the empyema still persists after the establishment of adequate and sufficiently prolonged drainage decortication may be considered. If this fails, thoracoplastic operations may be undertaken. The indications in the treatment of chronic and acute tuberculous empyema are the same.

HYDROTHORAX

Transudation of serous fluid into the pleural sacs is usually secondary to renal or cardiac disease. Renal disease gives rise to only small amounts but is often combined with cardiac insufficiency. Local stasis is probably a contributing factor in connection with new growths of the pleura, lung, or diaphragm. Occlusion of the azygos veins from pressure or thrombosis is a possible cause.

Cardiac insufficiency may give rise to fluid in one or both pleural sacs, with or without general dropsy. Cardiac hydrothorax is commonly unilateral and right-sided, and when both pleuræ are affected is usually greater on the right. Fetterolf and Landis¹ suggest that cardiac

¹ *Am. Jour. Med. Sci.*, 1909, **138**, 712.

hydrothorax is due to pressure on and partial occlusion of the pulmonary veins by dilated portions of the heart. The more common dilatation of the right auricle is responsible for the greater frequency on the right. Of 30 cases of cardiac hydrothorax the effusion was bilateral in 8, in 6 of which the amount of fluid was greater on the right and equal on the two sides in the remaining 2. It was unilateral and right-sided in 16, and confined to the left side in only 6. The predominance of right-sided accumulations is too constant to be accidental or to be explained by previous pleuritis and obliteration of the left pleura, which can account for only a small proportion of the cases. Hydrothorax from renal disease alone is usually bilateral. If, as often happens, the heart is insufficient, the accumulation may be unilateral and right-sided or double, with an excess on the right. Of 15 cases, the effusion was bilateral in 7, in 2 of which the amount was greater on the right, in 3 on the left, and equal on the two sides in the remaining 2. It was unilateral and right-sided in 6, of which 5 were complicated by cardiac lesions. The effusion was confined to the left side in 2 cases.

If the decubitus is prevailingly lateral, a larger amount of fluid may collect in the dependent pleura. The pleura may be smooth or slightly clouded and swollen. Old adhesions may limit the accumulation to single or multiple pockets. The fluid is usually clear and yellowish, but may be reddish from admixture of blood. It clots slowly or not at all, and fibrin is absent in uncomplicated cases. The specific gravity in venous transudates is usually from 1010 to 1015, with 1 to 3 per cent. of albumin, while hydremic fluids are below 1010, with traces to 1 per cent. of albumin. The sediment usually shows an excess of endothelial cells. In rare instances lymphocytes may predominate. A complicating pleuritis is not uncommon, and polymorphonuclear cells may then outnumber the other elements.

Symptoms.—The symptoms are those of the underlying disease and pain is absent. If there is fever, it cannot be ascribed to hydrothorax. Cough and expectoration may be due to œdema of the lungs. There may be gradually increasing dyspnoea, which may amount to orthopnoea. The signs are the same as with pleural fluid of other character. Pleuritic friction is absent. Shifting dulness is more readily obtained.

Treatment.—This is that of the underlying disease. Removal of the fluid by thoracentesis is indicated, if necessary, for relief.

HEMORRHAGIC PLEURAL FLUIDS

Microscopic blood is always present in pleural fluids. Small amounts may arise from puncture of the lung in thoracentesis. Larger quantities color the fluid reddish or even blood-red. From 5000 to 6000 red cells per cubic centimeter are necessary to give the fluid a definitely red color. Only cases with frankly hemorrhagic fluid are considered here. In old extravasations the fluid may be reddish-brown, yellowish or greenish. Clinically, it is convenient to divide bloody fluids into hemoserotherax (hemorrhagic pleurisy), hemohydrothorax, and hemothorax.

Hemoserothorax (Hemorrhagic Pleurisy).—**Primary.**—(a) *Tuberculous.*—An apparently primary disease of the pleura with the production of serohemorrhagic fluid is tuberculous in a great majority of cases. (b) *Malignant:* In a relatively small proportion of cases it is due to carcinoma, rarely sarcoma. A discussion of these causes will be found elsewhere. In both groups the effusion may become more bloody with successive tappings. (c) *Simple Hemorrhagic Pleurisy:* There is no sound evidence in support of this group as a primary affection, although hemorrhagic fluids of secondary and infectious origin are not uncommon. The clinical cases with an apparently primary hemoserothorax will be found to run practically always a clinical course consistent with tuberculosis or malignant disease, or show one or the other of these conditions at autopsy. There are a few striking exceptions as regards a more favorable clinical course. Osler referred to a large, able-bodied man, with hemorrhagic exudation, who was healthy and strong eight years afterward. Cheesman and Ely¹ reported a remarkable instance in a woman, aged forty-seven years, with bloody fluid first in the right, then in the left chest, and finally, following the disappearance of this fluid, with bloody serum in the abdomen. The pleural accumulations continued for about eighteen months, and no chest difficulty arose in the following seven years, but in this interval the abdomen was repeatedly tapped. The abdominal fluid ceased to reaccumulate after about five years, and at the date of the report twenty months had elapsed without recurrence. There was a large fibroid in the uterus. In all, 279 pints of fluid were removed.²

Secondary.—This is much more common. Cases due to tuberculosis, although they may seem clinically to be primary, are usually secondary. So, also, in hemorrhagic pleurisy due to malignant disease, the primary form is rare, that from metastasis relatively common. Secondary hemorrhagic serofibrinous effusions are perhaps most common in pneumonia, and are usually due to the pneumococcus. Of 157 cases of lobar pneumonia, showing pleural effusion at autopsy, in 6 the exudate was bloody. In none of these was there evidence of tuberculosis of the pleura. An inflammation of the pleura in malignant fevers (variola, typhoid) in purpura hæmorrhagica or complicating such asthenic conditions as accompany malignant disease, nephritis, cirrhosis of the liver or chronic heart disease, may be of the hemorrhagic variety, whatever the cause of the process in the pleura. Some prove to be tuberculosis; others are simple and due to the pneumococcus or pyogenic organisms, the blood in the exudate being due to passive congestion or the intensity of the local process.

An interesting feature of the hemorrhagic pleural fluids is the high percentage of eosinophiles which they may contain and the presence, also, of a large number of eosinophiles in the circulating blood. In a case of apparently primary disease of the pleura, the bloody pleural fluid showed no excess of eosinophiles, but contained enormous numbers of cholesterol crystals, while the systemic blood showed 6400 white cells, of which 20 per cent. were eosinophiles.

¹ *Am. Jour. Med. Sci.*, 1899, **118**, 162.

² I am informed that the patient is entirely well twenty-three years from the onset.

Hemohydrothorax.—Transudates may have a hemorrhagic character in cardiac or renal disease. Thrombosis of the thoracic veins or their occlusion by pressure of tumors is a possible cause.

Hemothorax.—This may be due to the rupture of intrathoracic vessels following the development of aneurism, their erosion by disease or injury by trauma. With rupture or ulceration of the aorta, the left pleura is more often the site of the hemorrhage. The pulmonary veins and the vena cava may rarely be the source. The rupture of pulmonary vessels from destructive pulmonary processes occasionally leads to hemorrhage into the pleural sac. The intercostal arteries may be eroded in disease of the pleura. There is a specimen (No. 2159) in the Warren Museum from a patient with empyema, in whom erosion of an intercostal artery led to fatal hemothorax.

Traumatic Hemothorax.—Etiology.—This may arise from contusions of the chest, more often from fracture of the ribs, and most commonly from incised or penetrating wounds. Of 21 cases (18 Massachusetts General Hospital and 3 private cases) 8 were due to automobile or other vehicle accidents, 6 to bullet wounds, 5 to falls, and 1 each to stab wounds and a coasting accident. The bleeding may come from injured vessels in the thoracic wall, more rarely from small branches of the parietal vessels. Owing to the protected position of the intercostal arteries, their injury is relatively uncommon. In a large proportion of cases the hemorrhage is from a wound of the lung, superficial injuries of which may lead to varying and usually insignificant hemothorax, deeper wounds to abundant hemothorax, if an important vessel is involved. The injury of vessels accompanying bronchi of the second or third order may be followed by hemorrhage compatible with survival.¹ Wounds of vessels about the hilus of the lung and the larger mediastinal vessels are followed by rapidly fatal hemorrhage.

Special Pathology.—Following the injury of the larger bloodvessels, fatal hemorrhage into the pleura may occur within a few minutes. An effusion of blood from the parietal vessels and the lung usually begins at once and is slowly continuous. In the more favorable cases the bleeding usually stops after twenty-four to forty-eight hours. Delayed hemorrhage is rare. Coagulation of the effused blood invariably occurs. It is frequently noted that hemorrhagic pleural fluid does not coagulate on removal, and this is probably due to its previous coagulation within the chest. Partial clotting may take place after removal.

In favorable and uncomplicated cases the fluid is wholly absorbed. The number of red cells progressively diminishes in the effused blood. The blood clot becomes adherent to the pleural surfaces, softening and organization take place, and after small extravasations, nothing but a few adhesions may remain. With large hemorrhages and much clot, more extensive adhesions and thickening of the pleura persist. The affected side may show diminished expansion.

The blood is not in itself a cause of pleuritis, and when infection occurs in hemothorax, it is due to bacteria which have invaded the pleural

¹ Nélaton: Des épanchements de sang dans les plèvres, etc., *Thèse de Paris*, 1880.

sac from without, through the thoracic wound or the lung. It is less frequent in small effusions, and is less likely to occur following injuries of the parietal vessels or the superficial parts of the lung, without an external wound. Large effusions of blood, those arising from incised or penetrating wounds, and hemorrhage from the deeper parts of the lung, often become purulent. In judging the presence of an infection from an enumeration and differential count of the white cells, due allowance must be made for the number of polymorphonuclear cells in the effused blood. Hemorrhagic pleural effusion following trauma may rarely be tuberculous.

Symptoms.—In small and slowly accumulating effusions there may be no symptoms. Shock is a variable feature. Pressure symptoms usually occur within twenty-four hours and are rarely delayed for forty-eight hours. In one of Nélaton's cases the hemorrhage was delayed for thirty-six days. With the rapid accumulation of a large amount of blood, death may ensue within a few minutes. In most cases there is slowly increasing dyspnoea, which is the most constant symptom, due to collapse of the lung and consequent dislocation of the mediastinum. Pain may be present, and is usually referred to the affected side. Cough is an inconstant symptom. If the lung is wounded there is likely to be hemoptysis. Blood in the sputum may consist of blood streaks, or there may be frank hemoptysis. In addition, with the more rapid accumulation, there are symptoms due to loss of blood, pallor, progressive elevation of the pulse, with alteration in its quality, coldness of the extremities and body, and sweating. Syncope or delirium may occur. The temperature may be subnormal at first and in favorable cases may not exceed normal limits. In a considerable proportion of cases the temperature rises, after the first or second day, 1° or even 2° F., and remains thus elevated for several days. Although such an elevation naturally occasions anxiety, such cases not infrequently progress favorably. The fever may be due to absorption. The physical signs differ in no respect from those with pleural fluids of other character.

Complications and Sequelæ.—Infection of the effused blood is most to be feared. There are no trustworthy statistics but it appears from Nélaton's 94 collected cases that the effusion became purulent with more or less certainty in 21. Hemopneumothorax is common, and may become pyopneumothorax. Pneumonia, pulmonary abscess, or gangrene may arise from the injury or follow as a result of neglected empyema.

Diagnosis.—A careful examination should be made when the patient first comes under observation. Neglect of this may lead to unnecessary delay in the diagnosis of empyema. A pleural effusion developing within a few hours of a thoracic injury means hemothorax with practical certainty; a delayed effusion is usually inflammatory, rarely hemorrhagic. The early detection of infection is most important. Its occurrence is usually indicated by fever, which commonly occurs from the third to the fifth day, and is accompanied by other symptoms of sepsis, such as are ordinarily seen in empyema. Symptoms of sepsis may develop, however, only after days or weeks have elapsed. The presence of an infection may be suspected when, even without fever, there is a delay in the absorption of the fluid, which in most cases progressively diminishes in amount,

and moderate effusions may be fully absorbed within a month. Any increase of a fluid which has previously reached a standstill should be regarded as due to inflammation and not recurrent hemorrhage, which is relatively uncommon. A count at intervals of the white cells in the systemic blood may be of value in the early recognition of suppuration. An initial leukocytosis may be due to hemorrhage alone.

Exploratory puncture and the withdrawal of sufficient fluid for diagnosis should be done. If the puncture is made at a distance from the original injury there is less danger of dislodging an occluding thrombus. The needle should be inserted toward the upper rather than the lower level of the fluid, to avoid a dry tap from penetration of the clot. If properly performed, and under aseptic precautions, the procedure is practically devoid of danger. The aspirated blood should be mixed with a few crystals of potassium oxalate to prevent clotting and on this fluid a red, white and differential count made. In developing or mild infections microscopic examination of the sediment may show an excess of polymorphonuclear cells and also that degenerative processes are at work, from their necrotic appearance. Aërobic and anaërobic cultures should be taken.

Prognosis.—Traumatic hemothorax is always serious. The site, extent and character of the original injury, the rapidity with which the hemorrhage takes place and the amount of effused blood are important factors. In some cases the effusion may be small and pneumothorax the significant feature. To these dangers that of infection is added. Of Nélaton's 94 cases of traumatic hemothorax, gathered from the older literature, death occurred in 49 from immediate or remote causes. There were 5 deaths in 21 cases in the writer's series. The seriousness of chest injuries, in general, can be gathered from the cases collected by Garré.¹ In 37 cases of pulmonary rupture the mortality was 63 per cent.; in 100 cases of punctured wounds, 38 per cent.; in 535 bullet wounds, 30 per cent. Hemorrhage, pneumothorax, and infection are the principal causes of death.

Treatment.—This presents a difficult problem. The majority recover under expectant treatment. The hemothorax if uninfected will be absorbed and removal of more than enough fluid to establish the diagnosis and settle the question of a complicating infection is undesirable for fear of dislodging an occluding thrombus and exciting renewal of hemorrhage. An opiate should be given if necessary to quiet pain or cough.

In a small proportion of cases, imminent danger of death from hemorrhage or encroachment on intrathoracic space or both raises the question of interference as a life-saving measure. Previous to the war the consensus of opinion was even in such cases in favor of conservative measures and the avoidance of operative interference. With alarming pressure symptoms, however, thoracentesis and the removal of small amounts of blood for the relief of pressure was deemed justifiable. Inasmuch as relief of pressure may promote further hemorrhage, the procedure is, if possible, to be avoided, at least within the first two to three days of the onset.

¹ *Arch. f. klin. Chir.*, 1905, **77**, 209.

Improvement in surgical technique and especially the use of differential pressure anesthesia has led to the adoption of operative measures for urgent indications in certain cases. Duval¹ in 300 cases of gunshot wounds of the chest, excluding operations of urgency, found a mortality of 20 per cent. under medical treatment and by contrast in 136 cases, of which 18 were urgent and 118 not urgent, treated by operation, a general mortality of 9 per cent. Sauerbruch² regards severe hemorrhage as an indication for surgical intervention and is influenced in the estimate of its severity by the clinical progress. Rapid extension of the area of dullness, increasing dyspnoea, more rapid pulse, more outspoken pallor, and a fall in temperature are danger signals against further delay in the postponement of operation. The chest is opened under differential pressure, the source of hemorrhage found and the bleeding stopped by the application of special clamps. Bleeding vessels are ligated, the clamps removed and the lung wound sutured. The pleural cavity is carefully sponged to remove the blood and after inflation of the lung the external wound is closed. The usual presence of a considerable degree of shock, the difficulty of estimating the spontaneous outcome and the risk of surgical intervention are likely to deter other than experienced thoracic surgeons from a resort to operation. The probable source of the hemorrhage may properly be considered in estimating the chances of successful surgical intervention. The more readily accessible parietal vessels may be suggested by the nature and site of the injury, but the lung itself is more often the source and the dangers and difficulties are then much increased. Most dangerous bleeding arises from the injury of hilus vessels. Sauerbruch³ reports four instances of bleeding from hilus vessels treated surgically with complete success.

External wounds should be thoroughly cleaned and disinfected by painting with iodine. Increase in the amount of fluid after the first few days suggests infection as a cause rather than further bleeding. Persistent fever may be due to absorption of sterile fluid but raises the question of superimposed infection and exploratory puncture may be necessary. If suppuration occurs the empyema should be opened and drained.

CHYLOTHORAX

Chylous and Chyliform Pleural Fluids.—Much confusion exists in the classification of milky fluids which accumulate in the serous sacs. Quinke,⁴ in 1875, grouped the cases into those with chylous fluid (hydrops chylosus) in which the appearance was due to the presence of true chyle, and a second class with a chylous appearance (hydrops chyliformis seu adiposus), the milky character being due to cells undergoing fatty degeneration. The distinction is often difficult and at times impossible. The two types may be present in different cases, both of which are due to a similar cause, and a single sample of fluid may present features common to both.

¹ *Surg., Gynec. and Obst.*, 1919, **28**, 1.

² *Chir. d. Brustorgane*, 1920, vol. 1.

³ *Chir. d. Brustorgane*, 1920, vol. 1.

⁴ *Deutsch. Arch. f. klin. Med.*, 1875, **16**, 121.

Such fluids are white and milky but may be reddish from the presence of blood or show varying shades of yellow or green. In the last instance they may readily be mistaken for purulent fluid. They are usually odorless, but may be slightly sweetish. Thin layers are opalescent. On standing, a creamy layer of fat collects at the surface. They are resistant against putrefaction. Their milky appearance is maintained after filtration or centrifugalization, but they can be cleared by shaking with ether. From 0.06 to 3.71 per cent. of fat has been extracted. The amount of albumin is variable; from 3.36 to 7.37 per cent. has been reported, with traces of casein in one instance. Solids are present from 5 to 10 per cent., inorganic substances (salts and extractives) about 1 per cent. Fibrin is variable, present in some, absent in other cases. Cholesterin, lecithin, calcium, magnesium, potassium, sodium, chlorine, and carbonic, sulphuric and phosphoric acids have been found. Microscopic examination discloses a large number of minute fat droplets about the size of micrococci. In the chylous fluids the fat granules are very numerous, with only few formed elements, while the chyloform fluids contain less numerous fat granules, of larger size, and more numerous cells in different stages of fatty degeneration.

Pseudochylous Fluids.—Pleural fluid, without fat, may have a milky appearance. Quincke showed that albumin in fine subdivision may cause a milky appearance. Lion,¹ in 1893, showed that fat was absent in a milky abdominal fluid which he studied. An albuminous body of uncertain nature was found. Such substances have been regarded as lecithin, globulin, casein or a compound of globulin and lecithin. These pseudo-chylous fluids are distinguished from the chylous and chyloform fluids by the separation of the latter into two layers on standing, while the former remain homogeneous. The microscopic examination of chylous or chyloform fluids shows the presence of fat, which may be stained black with osmic acid or removed by shaking with ether. In gross appearance chylous and chyloform fluids may resemble purulent fluids.

Occurrence.—Chylous or chyloform pleural fluids are of infrequent occurrence, but probably more common than the number of reported cases indicates, since chylous may be readily confused with purulent fluid, unless carefully examined. Bargebuhr² was able to collect 41 cases, reported from 1633 to 1894, an incidence of 1 case reported about every six years. Rotmann³ in 1896 brought the number to 49.

Etiology.—Of 40 cases in Rotmann's series, in which the cause could be determined, 27 were classed as chylous, 13 as chyloform. Of the chylous cases, 8 were due to trauma; 5 to cancer of the pleura; 4 to occlusion of the left subclavian vein. Two cases were ascribed to each of the following causes! Compression of the duct by tumors, disease of the lymph vessels (sclerosis, lymphangiectasis), and malignant lymphoma, and 1 case each as follows: Occlusion of the thoracic duct, excessive exertion and parasites (filaria?). The presence of chyloform fluid, with admixture of fatty degenerated cells, was due to cancer of the pleura,

¹ *Arch. de med. exper. et d'anat. path.*, 1893, No. 6, p. 826.

² *Deutsch. Arch. f. klin. Med.*, 1895, **54**, 410.

³ *Ztschr. f. klin. Med.*, 1896, **31**, 416.

lymph vessels, etc., in 5; tuberculous pleuritis in 3; exudative (non-tuberculous) pleuritis in 3; and pulmonary abscess (?) in 1. One case was regarded as the result of an abnormal amount of fat in the blood (lipemia?).

Diagnosis.—The chylous or chyloform character can be determined with certainty only by an examination of the fluid. Its presence may be suspected, however, following trauma, with malignant disease of the pleura, glands or lymphatics, and with thrombosis of the left subclavian vein. The association of pleural fluid with the known presence of chylous ascites may suggest a chylous character to the former. Uncomplicated cases of chylous or chyloform pleural fluid are usually afebrile. Such an accumulation may occur at any age and in either or both pleural sacs.

Prognosis.—*Chylous Fluids.*—The transudation of chyle into the pleura adds to the danger of the underlying disease from the additional tax on the patient from loss of food. Thus the course of an affection steadily progressing toward a fatal termination may be hastened. The rapidity and extent of the accumulation are important for the estimation of its effect. Small accumulations, the removal of which is unnecessary, probably add little to the danger of the original disease. The prognosis becomes more unfavorable when alarming pressure symptoms necessitate the repeated withdrawal of large amounts of chylous fluid. The underlying cause is usually of so grave a nature that in general the prognosis must be considered unfavorable. Of 22 cases (11 classed as chylous, 11 probably chylous) in Rotmann's series only 4 recovered. Of these, 2 were due to trauma, 1 to probable disease of the lymph vessels, and the last to an uncertain cause.

Chyloform Fluids.—The prognosis is more nearly that of the underlying cause, such cases being due to the fatty degeneration of existing cells.

In cases with chylothorax in which recovery has followed, it is probable that the chylous transudation has come from branches of the main thoracic duct or that the occlusion of the latter is compensated by an abundant collateral circulation. Slight lesions of the thoracic duct may heal and the duct remain patent.

Traumatic Chylothorax.—Such cases present features of special interest from their rarity and more favorable prognosis. Of 11 cases, in the literature, the chylothorax was double in 1 case, left-sided with right hemothorax in 1, right-sided with left pneumothorax in 1, and confined to the right side in the remaining 8 cases. The traumatic cases may be fatal from the original injury plus the mechanical effect of the pleural fluid, or in time from loss of lymph.

In 1 of the reported cases an injury to the thoracic duct followed a bullet wound. In the remaining cases the chylothorax was due to severe mechanical injury with certain or probable fracture of the ribs. In 2 of the 5 fatal cases the thoracic duct was injured by fragments of the tenth and eleventh dorsal vertebrae respectively. The mechanism of injury to the duct in the other cases is uncertain. In these cases the implication of the parietal pleura in the injured structures is indicated by the presence of chylous fluid in the pleural sac. Rupture of the thoracic duct may, however, lead to an accumulation of chyle outside the pleural sac provided

the parietal pleura is uninjured. Under these circumstances the mediastinum may be infiltrated or the parietal pleura dissected up from the thoracic wall.

Treatment.—This presents a somewhat different problem from other pleural fluids, since the diminution of pleural pressure favors reaccumulation and changes in pressure interfere with the healing of lesions of the lymphatic vessels. The repeated loss of large amounts of such fluid is a severe drain. It is best, therefore, in the presence of small amounts of fluid to keep the patient under observation after sufficient material has been withdrawn for diagnosis. Strapping the affected side may prevent an increase of the fluid by diminishing the respiratory changes in intrapleural tension. When an excessive amount of fluid has accumulated it must be evacuated by thoracentesis. If possible, operation should be delayed until the level of the fluid has ceased to rise. It is better to remove small amounts frequently than a large amount at one time. Because of the inaccessible site of the thoracic duct an attempt at suture is hardly likely to prove successful. An increase of intrapleural pressure to that of the atmosphere, following resection of a rib, may effect a cure. Thoracotomy was followed by recovery in 1 case and death in another.

TUMORS OF THE PLEURA

Benign Tumors.—These are rare and without a distinctive clinical picture. They usually run their course undetected during life and are first discovered at autopsy. In general they consist of tumors arising in neighboring organs which invade the pleura by encroachment, usually remaining extrapleural, at times projecting into the pleural space, but enveloped by its visceral or parietal layer.

Aberrant lung tissue may project into the pleural space. In a case described by Muus,¹ a smooth tumor the size of a walnut was found in the left pleural cavity, attached to the diaphragm and covered by diaphragmatic pleura. The tumor showed, on section, an alveolar arrangement. Small single or multiple cysts of the pleura are described by Stilling² and Zahn.³ Their walls contained cartilage and acinous glands, lined with ciliated epithelium, suggesting their origin from the bronchi. Emphysema may give rise to cyst-like structures projecting into the pleural cavity (bullous marginal emphysema). A specimen in the Warren Museum (No. 2142) shows such a bleb, the size of a horse-chestnut its walls composed of thickened pulmonary pleura, lined with delicate trabeculae and connecting with the bronchi. They may reach a much larger size. Their rupture may give rise to pneumothorax. Pulmonary adenoma, angioma or osteoma may invade the pleural sac. Fibroma may arise in the lung and similarly invade the pleura.

Lipoma.—Fatty tumors may in rare instances arise from the subpleural fatty tissue and project into the pleural sac. They are usually too small to give rise to symptoms or physical signs, and are discovered postmortem, growing from the costal, diaphragmatic or mediastinal fatty tissue as rounded or flattened, sessile or pedunculated masses. Fitz⁴

¹ *Virchow's Arch. f. path. Anat.*, vol. 176, 180. ² *Ibid.*, vol. 114, 557.

³ *Ibid.*, vol. 143, 173, 416.

⁴ *Trans. Assn. Am. Phys.*, 1905, 20, 57.

reviewed the literature and reported a case. In rare instances, lipoma of the thoracic wall may communicate with the subpleural space and project into the pleural sac. Such possible communication through the thoracic wall with the thoracic cavity should be borne in mind in operations for the removal of subcutaneous lipomas, as infection of the wound may readily lead to infection of the pleura.

Primary Malignant Tumors.—Carcinoma.—Although the term endothelioma has been most commonly applied, carcinoma seems more appropriate. The general character and histological appearance of the tumor do not, in general, sufficiently differ from carcinoma in other regions and its origin in the surface epithelium or lymph vessel endothelium is too uncertain to warrant a more distinctive term.

Occurrence.—This is a rare affection, of which some 40 to 50 cases are sufficiently well recorded to permit of acceptance.¹ It is probable that the condition has not infrequently escaped detection because of the readiness with which it may be confused with chronic pleuritis, without a microscopic examination of the tissue. The disease is more common between forty and fifty years of age, but the ages of the reported cases vary from ten to seventy-four years. Men are somewhat more frequently affected. In rare instances it has followed trauma to the chest wall.

Pathology.—The disease is usually unilateral occurs about equally on the two sides, although the right pleura has been somewhat more commonly involved. Rarely both pleurae are invaded. The entire pleura of one side may be increased in thickness to 1, 1.5, or even to 2 cm. In other cases only a part of the pleural sac is diseased. The affected region is usually diffusely invaded, is gray or grayish-yellow in color, and studded with discrete or confluent white, grayish or yellowish nodules, varying in size from a pin-head to a pea. More rarely the pleura is the site of larger, multiple and isolated masses of growth. At times there are no nodules; the pleural surface is merely uneven and apparently diffusely involved. The tissue is hard and tough on section. Ulceration is not found. Adhesions are common. A variable amount of bloody, less commonly serous, rarely purulent fluid is usually present.

Metastases have been observed in the supraclavicular and axillary glands and the thoracic muscles spontaneously or along the needle track, after withdrawal of pleural fluid. The disease has usually invaded other organs when death occurs. The most frequent site of secondary deposits is in the lungs. The bronchial, tracheal, mediastinal, retroperitoneal, and mesenteric glands, the viscera, other serous membranes, etc., may be the site of metastases. In 6 of the reported cases no metastases were found. In the presence of carcinoma elsewhere than in the pleura and especially with the disease in the lungs, it is never certain that the pleural disease is primary.

Symptoms.—The disease usually begins like an ordinary pleuritis, and in its course closely resembles pleural tuberculosis. Pain is usually a prominent symptom and is often increased by long breath and cough. Dyspnoea and cough are not usually striking features at first, but may

¹ Cases reported to 1897 have been collected by Glockner (*Ztschr. f. Heilk.*, 1897, vol. 18); to 1905 by Bloch, *Les néoplasmes malins primitifs de la plèvre*, Paris, Vigot Frères.

be present without invasion of the lung. In the presence of pleural fluid, dyspnoea may be extreme and orthopnoea may be present. If the lung is involved the sputum may contain blood. Fever is usually absent. Loss of flesh and strength is usually progressive.

An accumulation of pleural fluid is almost constant and the physical signs are such as are commonly found with pleural fluid from other causes, although certain additional features may permit a probable diagnosis. Progressive loss of flesh and strength will naturally suggest a severe disturbance. Absence of signs pointing to disease in the apices of the lungs, failure to find tubercle bacilli in the sputum, and an afebrile course may argue against tuberculosis. Metastases in accessible regions are important. Inoculation metastases in the needle track should always be sought in suspected cases. They are usually small, flat, hard, slightly movable and painless. Their excision and microscopic examination may be necessary to establish the diagnosis.

On examination, diminished expansion of the affected side may be a striking feature. During the early part of the disease the side may be more prominent, to appear somewhat smaller later, with relatively narrow and less depressed interspaces. With effusion, the heart may be displaced, returning at first to its former position after the withdrawal of the fluid. As the new growth gradually invades a larger territory and as the pleura becomes thicker and less elastic, with the formation of adhesions, the heart often fails to return to a position which it might be expected to assume after the removal of such an amount of fluid. For similar reasons, the thoracic distress and sense of pressure are afforded progressively less relief from the evacuation of the fluid, which reaccumulates more rapidly. The operator may also be able to appreciate the much thickened and tough pleura by the resistance offered in the introduction of the trocar. The physical signs may show little if any change after the removal of even large amounts of fluid.

Examination of the pleural fluid may afford important data for diagnosis. It is often serous at first, becoming blood-tinged or even strongly hemorrhagic after the first or the first few tapplings. This is due to the inelastic character of the pleural walls, and the presence of bloodvessels near the free surface of the pleura, from which under the influence of increased negative pleural pressure following removal of the fluid, blood is readily extravasated. With the progress of the disease and the frequent repetition of tapping, the fluid may resemble pure venous blood or have a chocolate color. The specific gravity is usually 1018 or under. Microscopic examination of the sediment may assist in a decision between malignant disease and tuberculosis. In carcinoma of the pleura there is usually a much larger proportion of endothelial cells, with a relatively small proportion of lymphocytes, the cytological formula thus conforming to that in fluids due to stasis. The presence of many cells showing typical or atypical mitoses has been thought diagnostic of malignant disease.

It may rarely happen that the microscopic examination of a small piece of tissue removed with the needle may establish the diagnosis.

Roentgen-ray Examination.—Uniform increase of density at the base on one side, reaching its highest level toward the axillary region with

obscuration of the diaphragm and displacement of the heart to the opposite side suggest the presence of pleural fluid. The absence of shadows suggesting tuberculosis at an apex may serve to suggest the possibility of neoplasm. Metastatic lesions in the lungs or mediastinum may afford additional evidence in favor of malignant disease.

Prognosis.—The disease usually terminates fatally within six months of the discovery of the pleural invasion but may last eighteen to twenty months from the beginning of symptoms.

Treatment.—This is largely symptomatic. Removal of the pleural fluid usually affords only temporary relief. At times it is followed by marked improvement, especially in the early stages. As the disease progresses, distressing pressure symptoms usually necessitate more frequent withdrawal, with less and less relief. At times, with much thickening of the visceral pleura, removal of fluid may only aggravate the symptoms, from increased tension on a retracted and adherent lung. Morphine in sufficient doses may prolong the necessary intervals between the tapplings. It is better to withdraw small amounts frequently than to empty the cavity at each tapping.

Sarcoma.—Primary sarcoma is even less common than primary carcinoma of the pleura. Although in some of the reported cases a distinction has not been made between the two groups, this is justified from the general character and histological appearance. Mehrdorf¹ reviewed the literature and Bernard² found 24 reported cases. Two cases have come under my observation. Of 14 cases which I have analyzed 9 occurred in males. The ages varied from seven to seventy-six years. Of the remaining patients, 2 were from ten to twenty, 4 from twenty to thirty, 2 from thirty to forty, 1 from forty to fifty, 2 from fifty to sixty, and 1 from sixty to seventy years of age. The two sides are about equally affected. In their clinical course they resemble primary carcinoma of the pleura. A collection of pleural fluid practically always accompanies the new growth, and is usually bloody, rarely serous. Its hemorrhagic character may first appear only after tapping. The presence of spindle cells in the sediment may suggest spindle-celled sarcoma of the pleura, as in Warthin's case.

In gross character at autopsy, primary sarcoma of the pleura usually presents a different appearance from primary carcinoma. In rare instances, however, as in primary carcinoma, the pleura may be diffusely and homogeneously invaded. Rarely, there are innumerable small nodules, but the new growth is commonly single, hard, or soft, its surface smooth or lobulated, in color white, gray, or reddish, of variable and usually considerable size, even at times reaching that of a man's head. The pleura may cover the growth which appears to arise in the subserous tissue. In other cases no traces of pleura can be found, and the tumor itself forms the lining of the pleural sac, yet ulceration is uncommon. Invasion of neighboring organs by extension or metastases in the lungs, the neighboring glands, ribs, vertebræ, liver, spleen or superficial parts of the body has occurred. In 3 cases no metastases were found. Garré³

¹ *Virchow's Arch. f. path. Anat.*, 1908, vol. 193.

² *Ibid.*, 1913, 211, 156.

³ *Verhandl. d. deutsch. Gesellsch. f. Chir.*, 1909, 38, 121.

removed a spindle- and round-celled sarcoma weighing 1250 grams from the left pleura.

Secondary Malignant Tumors.—Malignant disease of the pleura is more commonly secondary than primary. The tissue may be invaded by metastases from a primary malignant tumor in any part of the body, but pleural invasion is more common in malignant disease of the lung, mediastinum, thoracic wall or stomach. Metastatic new growths of the pleura do not usually produce a diffuse infiltration of the tissue. There are commonly several isolated nodules or masses and more rarely the pleura presents a generally nodular appearance. Pleural fluid may or may not be present, and this may be serous, but is more commonly bloody. In cases of pleural carcinoma secondary to the disease in the breast, the clinical picture, course and termination may resemble primary carcinoma of the pleura.

Of 178 cases coming to autopsy at the Massachusetts General Hospital with carcinoma in various regions, 10 showed secondary deposits in the pleura. Of 10 cases with carcinoma of the breast, the pleura was invaded in 4. Of 58 cases in which the disease was primary in the stomach, only 3 showed pleural metastases. In this series, carcinoma of the pleura was also secondary to the disease in the thymus and ovary. Of 42 cases of sarcoma, primary in various regions, the pleura was secondarily invaded in 9.

ECHINOCOCCUS DISEASE OF THE PLEURA

Etiology.—Following the ingestion of the egg of *Tænia echinococcus*, the embryo may migrate by way of the portal blood stream or biliary channels to the liver, thence through the diaphragm to the pleura. Infection may also be direct or by way of the lymph channels or the systemic circulation.

Special Pathology.—1. **Pleural Echinococcus.** The number of cases in which the disease is primary in the pleura is small. In the combined statistics of Neisser and Madelung, among 1179 cases, echinococcus was primary in the pleura in only 18 (1.5 per cent.). This report is based on 43 cases.¹ The right pleura was involved in 25, the left in 10; in 8 the site was not given.

The cyst is usually situated at the lower, but may be confined to the upper part of the pleural cavity. Pleuritis is uncommon. Enlargement of the sac gradually compresses or displaces neighboring organs. Perforation may occur into the lungs with evacuation through the bronchi; or the chest wall. Both are rare. The cyst may become infected, and present the appearance of an encysted empyema. The most common type is a single cyst or one sac containing daughter cysts (endogenous echinococcus). Rarely more than one cyst is found. It is uncertain whether unruptured cysts in parts distant from the pleura can lead to secondary pleural invasion. The weight of opinion is rather that multiple and isolated cysts are due to infection with more than one echinococcus embryo at the same or at different times. Auto-infection through rupture

¹ References for these cases were given in the second edition of this work.

of pulmonary or hepatic cysts, or the evacuation of daughter cysts into neighboring tissues and their further development may take place, but pleural infection with bacteria usually precedes or so quickly follows that unless operation is undertaken, death almost always occurs within a variable and usually short period.

2. **Parapleural Echinococcus.**—(a) *Intact Cysts.*—In this class the disease develops in neighboring organs, but encroaches upon and grows at the expense of the pleural space. The cases comprise those in which cysts are present in the peripheral parts of the lung, the upper part of the liver, or the region between the liver and the diaphragm; and more rarely echinococcus disease of the mediastinum, spleen or kidney. The clinical picture may be quite indistinguishable from primary pleural echinococcus. Subdiaphragmatic and especially hepatic cysts are most common and the diaphragm may be elevated to the second rib and even to the clavicle. In both the subdiaphragmatic and pulmonary forms the heart may be displaced laterally and the liver dislocated downward. The condition of the pleura in the presence of an echinococcus cyst in its neighborhood is variable and depends to some extent on the presence or absence of suppuration in the cyst. The visceral and parietal layers may be free, serous or purulent pleural fluid may be present, but partial or complete adherence of its layers is more common and more favorable, as rupture of the cyst may then fail to infect the pleural sac.

(b) *Perforated Cysts.*—According to Neisser's statistics, echinococcus disease of the liver breaks through into the respiratory apparatus in about 11 per cent. of the cases. Disturbances of the pleura from parapleural echinococcus are more common than from the primary disease. Depending on the previous condition of the pleura and the character of the cyst contents, rupture is followed by free or encysted, cystic, serous or purulent fluid. Suppuration is practically a constant feature. The perforation of an adherent pleura with invasion of the lung or bronchi is most common. Of 30 cases in Davaine's series only 9 ruptured into the pleura, 21 into the lung or bronchi. In Neisser's 60 cases the pleura was invaded in 16, the lung in 12, and the bronchi in 32. Hepato-pleural or hepato-bronchial fistule may result, and bile may be found in the pleural cavity or even be expectorated. An echinococcus cyst of the lung may likewise lead to free or encysted and usually purulent pleural fluid, following rupture. If the pleuræ are adherent the pulmonary cyst may evacuate externally. Rupture into the bronchi is, however, more common.

Symptoms.—In rare instances there may be no symptoms. In cases in which the disease is primary in the pleura the symptoms are usually those of a slowly growing intrathoracic tumor. Cough may be absent or present, with scanty mucoid sputum from an accompanying bronchitis. Dyspnoea is usually present and progressive. There may be pain with respiration, but this is not striking unless pleuritis is present. Fever is usually absent. Emaciation is not common in uncomplicated cases. The perforation of pleural cysts into the lung is rare. Septic pneumonia and even abscess and gangrene may follow. If there is free communication with the bronchi, clear cystic fluid may be expectorated. In this or in evacuated pus, hooklets or bits of cyst membrane may be

discovered. Rupture may occur through the chest wall, following atrophy of the intercostal muscles and erosion of the ribs. Spontaneous rupture is likely to occur if the cyst has suppurated. The perforation of parapleural echinococcus into the pleura is less common than into the lung. Rupture may take place without symptoms; in other cases the patient may be conscious of the rupture, which is followed by pain of a severe character, and if suppuration is present, as is commonly the case, there are chills and fever. Rupture may be spontaneous or induced by exertion or trauma. If sinuses connect with the liver, biliary coloring matter may be expectorated. Hepatic echinococcus cysts may perforate the pleura and be evacuated through the lung without characteristic elements in the sputum, in case the bile passages fail to connect with the cyst. Urticaria, severe symptoms of intoxication, even delirium, collapse and death may follow the rupture.

The *duration* of pleural echinococcus is difficult to determine. It may take from six months to a year for it to reach the size of the fist. Symptoms may arise only after it has attained a large size.

The signs are usually those of encysted pleural fluid. There is diminished expansion of the affected side, which is likely to be prominent, with obliteration of the normal intercostal depressions. The side may be dull or flat on percussion and in some cases it is possible to note an irregular or evenly curved arching of the upper border of dullness, the convexity of which is directed upward. The tactile fremitus and breathing are diminished or absent; the latter may have a bronchial quality. The voice sounds are diminished and agophony may be present. The signs are likely to be atypical. Between the involved area and the lung there may be an abrupt transition on auscultation to normal vesicular breathing. The liver or spleen may be displaced downward, the heart to the right or left. The presence of echinococcus cysts elsewhere may suggest a similar affection of the pleura.

Blood.—An *eosinophilia* may be confirmatory. Cabot collected 30 cases of hydatid of the liver, only 2 of which were negative. Of 20 cases in Welsh and Barling's series, all but 5 exceeded the normal.

Diagnosis.—Cases which occur in North America and Great Britain are for the most part in foreigners. A previous residence where the disease is prevalent and contact with dogs used for herding sheep may be suggestive. Positive data for diagnosis are furnished by the discovery of scolices, hooklets or cyst membrane. If perforation has occurred into the lung, such material may be present in the expectoration. An urticarial rash following thoracentesis is very suggestive. The examination of the fluid obtained by puncture may furnish suggestive chemical features. It is usually clear, transparent, and varies from 1009 to 1012 in specific gravity. Sodium chloride is present. Albumin is usually absent or present only in traces. In some cases the specific gravity is high and the amount of albumin considerable. Cholesterin crystals may be found. Infection may mask the appearance of the fluid. Specific antibodies in the blood of patients with echinococcus disease may be demonstrated by the complement-fixation test.

Thoracentesis for the diagnosis of pleural or pulmonary echinococcus is attended by considerable danger. Perforation of the enveloping connective-tissue sac and the cyst membrane may result in the evacuation of the cyst fluid into the pleura or the lung, if erosion of its substance has already occurred. As the perforated cyst membrane is subjected to changes of intrathoracic pressure with respiration or cough, the contained fluid may find its way between the connective-tissue envelope and cyst membrane to the bronchi. Urticaria, severe intoxication, with gastro-intestinal disturbances, faintness, collapse, delirium, and even coma and death may result. Pulmonary or pleural suppuration or suffocation from mechanical obstruction by fluid or cysts may occur. Maydl reports 11 cases of pleural or pulmonary echinococcus in which a fatal result followed thoracentesis. Considering the infrequency of the disease, this is a warning which cannot be safely disregarded. If the diagnosis can be made without puncture it is better to resort to operation without previous exploration. If thoracentesis is done, a small trocar (not a needle) is less dangerous, and if the case proves to be echinococcus, operation should at once be undertaken.

Prognosis.—This is practically hopeless for echinococcus cysts of the pleura or parapleural tissue rupturing into the pleura, and allowed to run their course without treatment. Of 31 unoperated cases in Neisser's "statistics," including 12 pleural, 7 pulmonary with pleural perforation, and 12 hepatic with pleural perforation, all died. The prognosis is much worse for pleural than pulmonary echinococcus in which perforation into the lung may be followed by recovery. The prospect with operation is much more encouraging. Of 13 cases of pleural echinococcus in Maydl's statistics operated on, 4 (30 per cent.) died.

Treatment.—Evacuation of the cyst contents with the trocar, with or without the injection of solutions containing iodine or other substance, has been followed by cure, but is too dangerous to recommend. The high mortality following puncture of the cyst has been mentioned. A radical operation only can be considered. Costatectomy is better than simple incision. If possible, the cyst should be removed without rupture. If too large to be removed entire, the cyst membrane may be drawn into the wound of operation and aspirated. It may then be shelled out from its capsule. As it is often difficult to be certain that the cyst is not pulmonary or subdiaphragmatic, the pleura should be carefully approached. The use of differential pressure anesthesia is desirable when the pleural sac is free to prevent lung collapse. If suppuration of the sac has taken place, the abscess should be opened and drained as in other suppurative pleural affections. Subdiaphragmatic cysts projecting into the thorax are best approached through the pleura.

CHAPTER IX

PNEUMOTHORAX

By FREDERICK T. LORD, M.D.

By this is understood the presence of atmospheric air or gas in the pleural cavity. There is also frequently a liquid exudate, hence the terms hydropneumothorax with serous, pyopneumothorax with purulent, and hemopneumothorax with bloody fluid.

Historical Note.—The splashing sound produced by succussion is mentioned in the works commonly ascribed to Hippocrates and is frequently spoken of as “Hippocratic succussion,” but the condition in which it was noted was regarded as empyema, the distinction between empyema and pneumothorax not being clearly appreciated. A few cases were described, usually of the traumatic variety, and the mechanics of pneumothorax were fairly understood in the seventeenth and eighteenth centuries, but the thesis of Itard¹ in 1803 is commonly regarded as the starting-point of the modern conception of the disease. Itard named the condition pneumothorax and recognized its relation to tuberculosis. In 1819 Laennec published the most important contribution up to that time. He described the causes, symptoms, and physical signs, and his account of the auscultatory phenomena left practically nothing to be added by those who have since written on this subject. He was the first to give the succussion splash its true significance. Emerson² in 1903, published the most elaborate and complete treatise on the disease and gave an abstract of many important articles.

Pathological Physiology.—The lungs are not only easily distensible but are elastic and are stretched in both phases of respiration beyond the volume they would assume if the pleural cavity were open and in free communication with the external air. Owing to the constant elastic tension of the lungs there is in the potential pleural space a negative pressure which is greater during inspiration than in expiration. Many attempts have been made to measure this normal intrapleural tension after death in man and on living animals, but the results of such observations cannot be regarded as indicating the condition in healthy man. Aron,³ found as an average of 36 observations the maximum reading for quiet inspiration —5.09 and the minimum for expiration —2.54 mm. Hg. in a healthy individual willing to allow a manometer to be inserted into the chest. This normal tension thus demonstrated probably varies within wide limits in different individuals. Pleural adhesions or disease in the lung and mediastinum are likely to influence the pleural pressure and may explain the wide differences in the measurement of intrapleural tension by different observers and in the clinical behavior of cases of pneumothorax.

¹ Dissertation sur le pneumothorax ou les congestions gazeuses qui se forment dans la poitrine, Thèse, Paris, 1803.

² Pneumothorax: *Johns Hopkins Hosp. Rep.*, 1903, vol. 11.

³ *Die Mechanik und Therapie des Pneumothorax*, 1902.

Owing to the elastic tension of the lung and the consequent negative pressure in the potential pleural space, the admission of air to the pleural cavity is followed by collapse of the lung. The mechanical conditions differ somewhat, depending on whether the communication of the pleural space with the outside world is open, valvular, or closed.

Intrapleural Pressure in Pneumothorax.—Observations are not numerous. Among them Aron reported 3 cases illustrating each form. In a patient operated on for empyema with an open external fistula the pressure oscillated about the zero point, with an average of -2.62 mm. Hg. during inspiration and $+1.01$ during expiration. In a case of valvular pneumothorax, the average pressure at the height of inspiration was $+7.93$ mm. Hg., during expiration $+10.48$. In a patient with closed pneumothorax the pressure in inspiration was $+0.4$, in expiration $+5.0$. A positive pressure at the height of inspiration as in this case suggests the diagnosis of closed pneumothorax. Among West's¹ 20 cases of pneumothorax the highest pressure was 9 inches of water (17 mm. Hg.).

Incidence.—The cases occur more commonly between the ages of twenty and thirty, corresponding to the period when pulmonary tuberculosis is most frequent. The condition occasionally occurs in children but is rare under three years of age. It may occur as the result of trauma in efforts to resuscitate the new-born. Males are more frequently affected, probably because subjected to greater physical exertion. In James's² series of 125 cases, 103 were males. Statistics vary as to the frequency with which the two sides are affected. It seems to be somewhat more common on the left.

Etiology.—There are three groups: (1) The air may come from a perforation of the pulmonary pleura and the lung, bronchi, trachea œsophagus, stomach or intestines, forming an internal fistula. (2) Air may enter the pleura through a perforating wound of the outer chest wall, forming an external fistula. In both groups atmospheric air is admitted. (3) Gas may be generated by decomposition of a pleural exudate.

The commonest cause is disease of the lung, and in the majority of the cases there is tuberculosis. Among Biach's 918 cases³ from three Vienna hospitals 715 (77 per cent.) were due to pulmonary tuberculosis. In Drasche's 230 cases,⁴ 198 (86 per cent.) were ascribed to this cause; of Mosheim's 50 cases,⁵ 42 (86 per cent.). Thus from 80 to 90 per cent. may be regarded as tuberculous.

The incidence of pneumothorax among patients with pulmonary tuberculosis was 36 (10.1 per cent.) among 355 cases which came to autopsy in Weil's series. West⁶ estimates it as 5 per cent. of the fatal cases. In large series of clinical cases the proportion is lower, as among Drasche's 10,212 cases⁷ of pulmonary tuberculosis in which there were 198 (1.93 per cent.) with pneumothorax.

¹ Intrapleural Tension, *Allbutt's System of Medicine*, 1899.

² Osler's *Modern Medicine*, 1st ed., 1907, **3**, 870.

³ Zur Aetiologie des Pneumothorax, *Wien. med. Wchnschr.*, 1880, vol. **30**.

⁴ *Wien. klin. Wchnschr.*, 1899, No. 45, 117.

⁵ *Beitr. z. Klin. d. Tuberk.*, 1905, **3**, 331.

⁶ A Contribution to the Pathology of Pneumothorax, *Lancet*, May 3, 1884.

⁷ *Wien. klin. Wchnschr.*, 1899, No. 51, 1277.

Pneumothorax occurs more often in active than in latent, inactive or arrested tuberculosis. Most cases are due to the rupture of small subpleural tubercles which break down before communication with the pleural cavity is prevented by the formation of adhesions. Its infrequency with large cavities and in the more chronic types of the disease is due to more extensive and firmer pleural adhesions in these forms. The apex of the lung, though the most common site of cavity formation, is seldom the seat of the rupture owing to the frequency with which pleural adhesions obliterate the pleural sac in this region. Rupture of the pleura may occur during a violent effort, as coughing, lifting or sneezing, but in many cases there is no apparent immediate cause and the patient may be at rest in bed. In 23 cases with sudden onset (M. G. II.) the pneumothorax occurred while the patient was sitting still or in bed in 14.

Of other diseases of the lung in which pneumothorax may occur, abscess or gangrene and bronchiectasis as a group stand next in frequency, but the cases are rare. Pulmonary infarction may be the underlying cause. Bach¹ reports 3 cases and collected 31 from the literature in which emphysema was a certain or probable cause. There were 15 autopsies, and pulmonary tuberculosis was present in 5. Tumors of the lung and echinococcus disease are rare causes. Abscess and hydatid disease of the liver, ulcer or cancer of the stomach, cancer of the œsophagus, and perforation of the œsophagus by a fish bone have been recorded as causes. Spontaneous erosion and perforation of the lung or the chest wall by an empyema in rare instances cause pneumothorax.

Pneumothorax may be caused by a *penetrating wound* of the chest wall or of the lung, such as stab or gunshot wounds, but it is surprising how seldom this complication occurs. Among 21 cases of penetrating wounds of the chest in Bach's series there were no instances of pneumothorax. In fractures of the ribs a fragment of bone may injure the lung and produce pneumothorax. In James' 127 cases 11 were due to this cause. Occasionally a marked concussion of the body may rupture the lung and cause pneumothorax without external wound or rib fracture. Hemothorax is a frequent complication in traumatic pneumothorax. Empyema operated on in the ordinary way is converted into open traumatic pneumothorax.

The operation of *thoracentesis* may be responsible. A considerable number of cases have been reported. Sears² in 1906 was able to find references to 50 cases. Injury to the lung by the point of the instrument is rarely a cause. Faulty technique and the entrance of air through the cannula or needle is common, radiographic examination not infrequently indicating the presence of pneumothorax after the partial aspiration of pleural fluid. The amount admitted in this way is ordinarily small and no unfavorable symptoms usually ensue. The use of an air-tight trocar diminishes this danger. Misapplication of the tubing to the aspiration pump of Potain's apparatus so that air under positive pressure is blown into the chest has caused immediate death. The rupture

¹ Ueber das Vorkommen des spontanen Pneumothorax bei Emphysem, *Beiträg. z. Klin. d. Tuberk.*, 1910-1911, **18**, 21.

² *Am. Jour. Med. Sci.*, 1906, **132**, 850.

of pleural adhesions, an emphysematous vesicle or superficial pulmonary cavity by an excess of negative pressure during the aspiration of pleural fluid is probably the most common cause of the more serious types of pneumothorax in this group.

There is a small group in which pneumothorax occurs in apparently healthy individuals after unusual exertion, at times after laughing, crying, coughing, sneezing or yawning, and in rare instances while at rest and even asleep. There may be nothing to suggest tuberculosis and the pneumothorax is rarely complicated by an effusion. This is the so-called *spontaneous or idiopathic pneumothorax*. Fussell and Riesman¹ reported 2 and collected 56 cases. Young adults are most frequently affected. Death rarely follows and the pathology is not definitely known. Latent tuberculosis, the rupture of an emphysematous vesicle or the tearing of pleural adhesions are to be considered. The frequency of tuberculosis as a cause of other types of pneumothorax makes it necessary to exclude it most rigorously before any other explanation can be accepted.

Finally there are a few cases in which pneumothorax appears to be due to a gas-producing organism in pleural fluid.

Pathology.—If there are no pleural adhesions and the opening into the pleura is large, the lung collapses and retracts to a varying degree and may be found at autopsy as a shrunken mass lying against the spinal column. In long-standing cases it may be tough, fibrous, and practically airless with little resemblance to the normal lung. Tuberculosis with cavity formation is usually present. Pleural adhesions may bind the lung at one or more places to the chest wall. In some instances air is confined to a portion only of the pleural space, giving rise to partial pneumothorax. Confinement to an interlobar space without contact with the periphery of the lung was observed at autopsy by Monnier.² Such instances are extremely rare.

The perforation can usually be demonstrated and commonly leads into a large or small tuberculous cavity at the periphery of the lung. The hole may be several centimeters in diameter or so small as to be discovered only after the inflated lung is submerged in water. The perforation is usually single, but in rare instances two or more are found. In Roe's case³ a left-sided pneumothorax was due to perforation of the right lung through an adherent mediastinum. An inflammatory exudate may occlude the perforation, converting an open into a closed pneumothorax.

Air alone does not act as an irritant to the pleura, but pneumothorax usually arises under conditions in which bacteria readily gain entrance to the pleura, and it is only in exceptional instances, such as spontaneous pneumothorax or in rapidly fatal forms, that pleurisy fails to complicate the process. An exudate usually forms and according to West⁴ is serous, seropurulent or purulent, each in about one-third of the cases. Purulent exudates are common in children and following rupture from the alimentary canal. Hemothorax is not infrequent in traumatic cases.

¹ *Am. Jour. Med. Sci.*, 1902, **124**, 218.

² *Gaz. méd. de Nantes.*, November 2, 1907, 897.

³ *Med. Times and Gaz.*, 1866, **i**, 367.

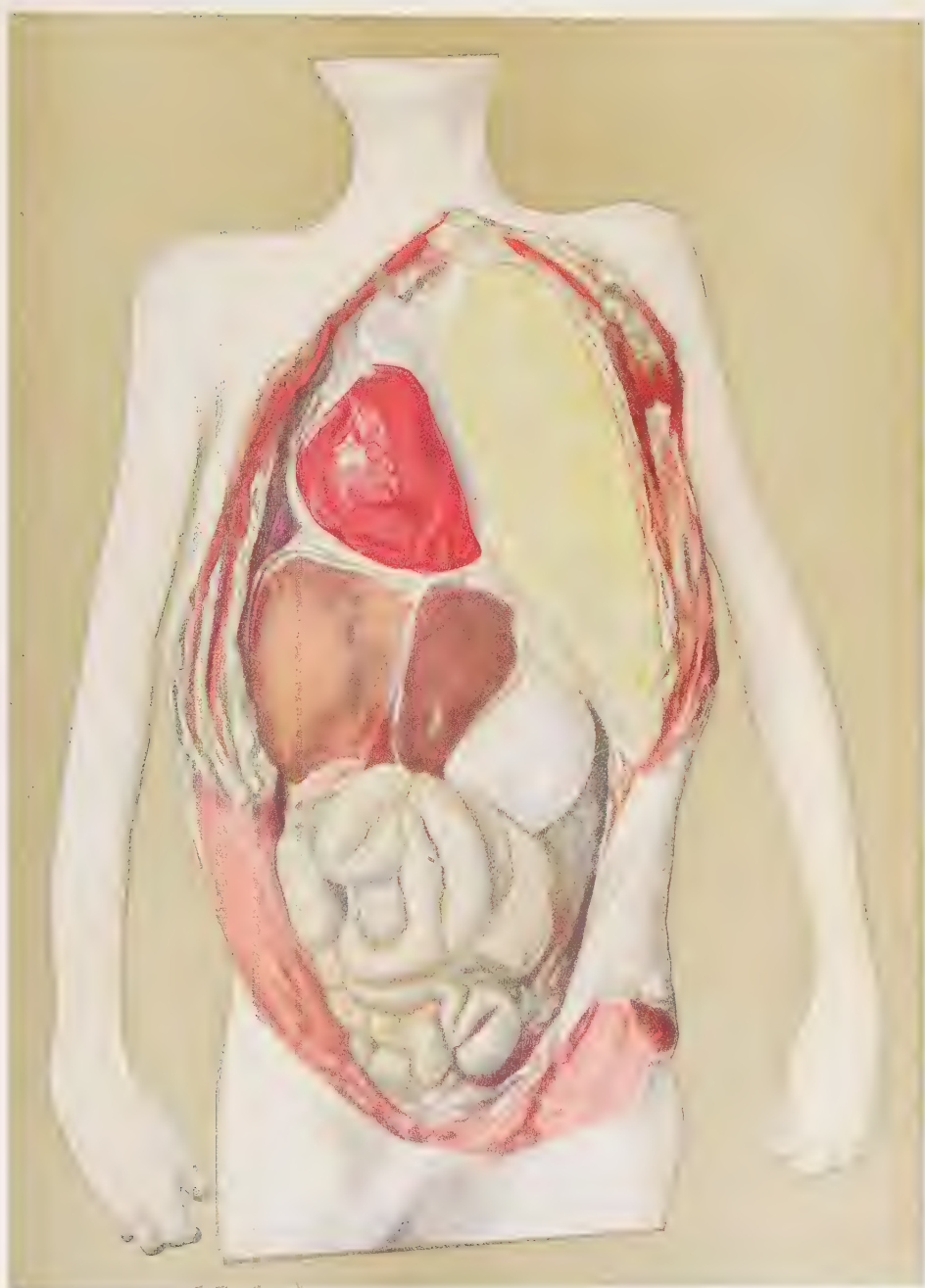
⁴ *Lancet*, 1887, **i**, 1264.

PLATE IV



Pyopneumothorax—Right Side. (James.)

PLATE V



Pyopneumothorax Left Side. James.

The mediastinum and heart are moved to the opposite side unless held by adhesions. According to James' observations and contrary to the general impression, the heart is not rotated or swung from its point of attachment at the root of the great vessels, but carried bodily across to the opposite side, its long axis maintaining about its normal relation to the long axis of the body. Encroachment on the sound lung follows the displacement of the mediastinum. Dislocation of the heart is greater with left than with right-sided processes. The position assumed by the heart and abdominal organs is well shown in the accompanying plates from photographs taken at autopsy. (See Plates IV and V.)

Symptoms.—Sudden onset is relatively uncommon. Of 64 certainly or probably tuberculous cases (M. G. II.) the onset was sudden in 23. Much depends on the local conditions. The initial symptoms are most severe when there are no pleural adhesions and the lung and mediastinum are free from disease, permitting complete collapse of the lung and dislocation of the mediastinum toward the sound side. The most alarming onset is therefore likely to be observed in early tuberculous cases, in traumatic or in spontaneous pneumothorax. Noteworthy symptoms are usually lacking when it occurs as a complication of empyema rupturing through the lung or following thoracentesis for the removal of pleural effusion.

Symptoms when present are most commonly pain in the affected side and sudden and severe or rapidly progressive dyspnoea. In uncomplicated cases there is slight and unproductive cough. If there is considerable purulent material in an infected lung more abundant sputum may follow its expression from pulmonary cavities or the bronchi. The rupture may be felt or be audible to the patient. The symptom-complex may simulate angina pectoris.

A typical severe attack like the following is occasionally observed. Thus, in a person previously in apparent good health there may be sudden, sharp pain in the chest, an immediate intense feeling of suffocation and fear of impending death, air-hunger, and great restlessness; the face at first pale and later cyanotic; the hands and feet cold and blue; the skin bathed in cold sweat. The *alae nasi* dilate, the respirations are rapid, and the accessory muscles of respiration are brought into play. The patient is usually found in the sitting position and if able to speak may plead in a scarcely audible voice to be taken to the open window. The pulse is rapid, small, feeble, or imperceptible. In 5 of 83 cases (M. G. II.) the attack was followed by unconsciousness, which terminated in death in 1 instance.

In milder cases there may be only slight pain and an increase of dyspnoea, the patient meanwhile not being incapacitated. In 4 cases (M. G. II.) the succussion splash was the first intimation to the patient and the principal complaint. In the majority of cases the occurrence of pneumothorax leaves no striking impression on the clinical aspect or is indicated only by an aggravation of existing symptoms. This is due to its usual occurrence late in the course of pulmonary tuberculosis when the lung is already considerably involved and the pleural sac partially obliterated by adhesions. In many cases the condition is unsuspected and discovered only in the course of the routine examination.

Signs.—These are commonly striking and distinctive. Small amounts of air may readily escape detection, however, and be first noted in the roentgen-ray examinations.

Inspection.—Immediately following the entrance of a large amount of air into the pleura the patient usually finds the sitting or half-sitting position most comfortable. In rare instances, as in Garde's remarkable case¹ the knee-elbow position is assumed, probably to prevent the disturbance incident to backward displacement of the heart. In this instance it was maintained for about fifty-six days (!). The decubitus in the more severe cases is likely to be on the affected side. Immobility, distention, flattening or fulness of the intercostal spaces, and absence of the diaphragm shadow may be noted. Weil reported œdema of the hand on the affected side, Zahn,² of the chest wall. Subcutaneous emphysema, at times of an extreme grade, is occasionally seen in traumatic cases or following thoracentesis. Dislocation of the heart away from the affected side is an important early sign and may be indicated by a visible cardiac impulse to the right or left of its normal position, the displacement being most marked in left-sided cases.

Palpation.—Vocal fremitus is much diminished or abolished over the involved region. In 70 of James' series in which this was noted above the level of fluid, it was diminished in 52 and absent in 18 cases. Vocal fremitus is usually absent over fluid. With a large amount of air the intercostal spaces are wider than on the unaffected side. Palpation may also establish the position of the displaced cardiac impulse and that of the depressed liver or spleen.

Mensuration.—This may show enlargement of the affected side; but the side may look larger and this fail of confirmation with the tape or the affected side may measure less than the other.

Percussion.—The percussion note is largely dependent on the size, shape, and tension of the air-holding cavity, the position of the retracted lung, the presence of adhesions, character of the pneumothorax, whether open or closed, and the presence or absence of fluid. The condition of the pleura appears to have no striking or constant influence on the percussion sound and it is sometimes difficult or impossible to explain variation in different cases or in different parts of the chest. The percussion note is usually strikingly loud, of low pitch, and may be described as hyperresonant and such as is obtained over an emphysematous lung. If the pneumothorax is large and the pleura free from adhesions hyperresonance may be determined to extend beyond the limits of the normal lung, exceeding the middle line toward the unaffected side over the mediastinum and invading or abolishing the hepatic or splenic dulness. The cardiac dulness also disappears or changes its position. In open pneumothorax there may be a tympanitic note. In some cases the resonance is defective or dull. The percussion note may have an amphoric quality.

With total pneumothorax, the retracted lung lies along the spine and is not demonstrable by percussion but if adhesions bind it over a larger or smaller extent to the chest wall the percussion note is impaired over

¹ *Arch. gen. de méd.*, 1828, **17**, 345.

² *Virchow's Arch. f. path. Anat.*, 1891, p. 123.

the adherent area. Defective resonance from this cause is frequently demonstrable at the apex, may be found along the spine posteriorly, and at times in other parts of the chest. The occasional presence of areas of tympanitic resonance below the level of fluid may be due to pleuritic adhesions.

Other modifications are at times observed. A cracked-pot sound may be obtained, due either to proximity of a pulmonary cavity to the chest wall or communication of a large open fistula with the pleural cavity. Inconstant changes in the percussion note with the mouth open or closed, on change of posture, during inspiration or expiration, and before or after aspiration may also be noted.

A small amount of pleural fluid complicating pneumothorax and concealed in the hollow of the diaphragm may not be demonstrable by percussion although detected by succussion. Dulness or flatness is generally present over large effusions but the amount is frequently underestimated, and Skoda's suggestion, *i. e.*, to estimate the amount of fluid in pneumothorax double that indicated by percussion will prevent some mistakes. The upper level of fluid is not always easy to determine and is likely to be placed too low, so that a needle introduced for the removal of air may be below the level of fluid. Marked mobility of the dulness over fluid and the constant maintenance of a horizontal upper border, in whatever position the patient is placed, are important and characteristic features of pneumohydrothorax, in striking contrast to the relative immobility and curved upper limit of dulness in pleural effusions without air.

Auscultation.—Suppressed or absent breathing with hyperresonance on percussion is usually the first indication in the examination that pneumothorax exists, and this diminution in the respiratory murmur is the more striking in contrast to the exaggerated breath sounds over the uninvolved lung. Diminished bronchial breathing may also be heard. The voice sounds and the whisper are diminished or absent. Among 90 of James' cases in which the character of the respiratory murmur was noted it was found to be diminished in 41, amphoric in 31, absent in 12 and bronchial in 6 cases.

Amphoric Phenomena.—The breathing not infrequently presents a peculiar metallic quality resembling the sound produced by blowing over the mouth of an empty decanter and hence spoken of as amphoric. This was first described by Laennec as "*bourdonnement amphorique*," and ascribed to the motion of the air in and out of the pleural cavity through an open fistula. In support of this explanation it may be said that an open fistula exists in most of the cases in which amphoric breathing is heard and the point of maximum intensity of the amphoric breathing over the chest is occasionally observed to coincide with the position of the fistula found at autopsy. The factors leading to the production of this sound have been the subject of much controversy and cannot yet be regarded as settled. The report of cases by Maréchal,¹ West² and Emer-

¹ *Jour. hebdomadaire de médecine*, Paris, 1829, 2, 116.

² *Trans. Clin. Soc.*, London, 1884, 17, 56.

son¹ in which amphoric respiration was present yet the fistula was certainly or probably closed, Powells' observation² of amphoric respiration over a distended stomach and Hoover's finding³ of amphoric respiration over a loop of distended intestine in the left hypochondrium suggest that a communication with the pleural cavity is unnecessary. The most probable explanation seems to be that the sound is due to the resonating properties of the pneumothorax cavity and is produced by the vibration of air within the cavity itself or by vibrations propagated from neighboring parts of the lung or bronchial tree. The presence of fluid is unnecessary for its production. It is variable in its location, intensity and pitch. Not only the respiratory murmur, but also in occasional instances the percussion note, cough, vocal resonance, whisper, the heart sounds, rales, pleural friction and deglutition sounds may have a metallic and amphoric quality.

Metallic Tinkle.—This is impressive and characteristic, and described by Laennec as resembling the sound produced by gently striking with a pin or dropping sand into a glass, metal, or porcelain vessel; or like the vibration of a metallic cord touched by the finger. Several explanations of this curious phenomenon have been offered. Agitation of the fluid against the walls of the pleural cavity, the bursting at the surface of fluid of bubbles of air which enter through a submerged fistula, the falling of drops from the walls of the cavity above to the surface of the fluid below or the modification by a suitable resonance chamber, such as the pneumothorax cavity, of rales produced in its vicinity have been suggested. The finding of metallic tinkling in cases in which from the absence of the succussion splash there was reason to believe that fluid was absent, as in those reported by Finny⁴ and Maillart and Laserre⁵ lends support to the last mentioned view, but as small amounts of fluid may fail to give this sign this explanation cannot be accepted without more conclusive evidence of the absence of fluid. The failure of Forbes⁶ to find on dissection any communication between the bronchi and the pleural fluid in a case in which metallic tinkle was most distinct suggests that the open fistula is unnecessary. The sound may be heard during respiration, speaking or coughing or after change of position. In some instances a cough may be needed to produce it and in doubtful cases this should be tried. At times metallic tinkling is audible to the patient and in Allbutt's⁷ remarkable case it could be heard for two hours in all parts of a large room. In James' series it was present in 30 and absent in 5 of 35 cases. Amphoric breathing may or may not be present with it. The sign is not distinctive of pneumothorax but may be heard also over large pulmonary cavities. Hérard⁸ heard metallic tinkling over a dilated kidney containing pus and gas. The ureter was patent.

¹ *Johns Hopkins Hosp. Rep.*, 1903, vol. 11.

² *Lancet*, 1882, i, 351.

³ *Cleveland Jour. Med.*, 1898, 3, 45.

⁴ *Dublin Jour. Med. Sci.*, 1898, 105, 273.

⁵ *Rev. méd. de la Suisse*, November 20, 1902.

⁶ Translation of *Laennec's de l'auscultation méd.*, 1834.

⁷ Finlay: *Pneumothorax*, *Allbutt's System of Medicine*, 1899, 6, 378.

⁸ *Bull. et mém. Soc. anat. de Paris*, 1850, 25, 98.

Succussion Sound.—In the works formerly ascribed to Hippocrates it is recommended "Seat him on a seat which will not stir. Let some one hold him by the arms while you shake him by the shoulders and listen to hear on which side the sound is produced." The sound resembles that produced by shaking a flask half full of water, and like other sounds heard in the chest with pneumothorax may have a metallic or amphoric quality. It is the earliest and most important indication of fluid and gas in the pleural cavity and may be obtained long before fluid can be demonstrated by other means. Small amount of fluid may fail to give the splash. Its intensity is variable. It may be heard only by the most attentive auscultation or readily audible to the examiner and even to the patient or in some instances appreciated in all parts of a large amphitheatre, as in James' case of left pyopneumothorax (Plate V). At times it may be heard only with the patient erect or only in the recumbent position. In 54 of James' cases it was present in 41, absent in 13 cases. Similar splashing sounds may be obtained from the stomach, the intestine or the peritoneum if fluid and air are present, but the site of maximum intensity and other evidence usually serve to exclude errors from these sources. In some instances it may be necessary to be sure that the stomach is empty when the test is made. The churning "mill-wheel" murmur of pneumohydropericardium can hardly be a cause of confusion. Some difficulty may be experienced in differentiating pneumohydrothorax from a pulmonary cavity containing air and fluid.

Coin Sound.—This is known also as the bell sound and Bruit d'Arain. It was first described in an anonymous article,¹ which attributes its discovery to Trousseau. The test is usually made by having an assistant place on the chest a coin against which another is struck, while the examiner listens with the ear or stethoscope at a point on the chest wall directly opposite. If present, a clear, musical, bell-like tone is produced, resembling in its quality the amphoric phenomena previously described and quite different from the sound over the unaffected side. Among 25 of Emerson's cases it was present in 20, absent in 3, suggestive in 2. In 37 of James' series, it was present in 25, absent in 12. This sound, like amphoric breathing, is probably due to the peculiar resonating qualities of the pneumothorax cavity. It is not absolutely distinctive of pneumothorax. Osler² reported its presence over a large cavity in the right upper lobe.

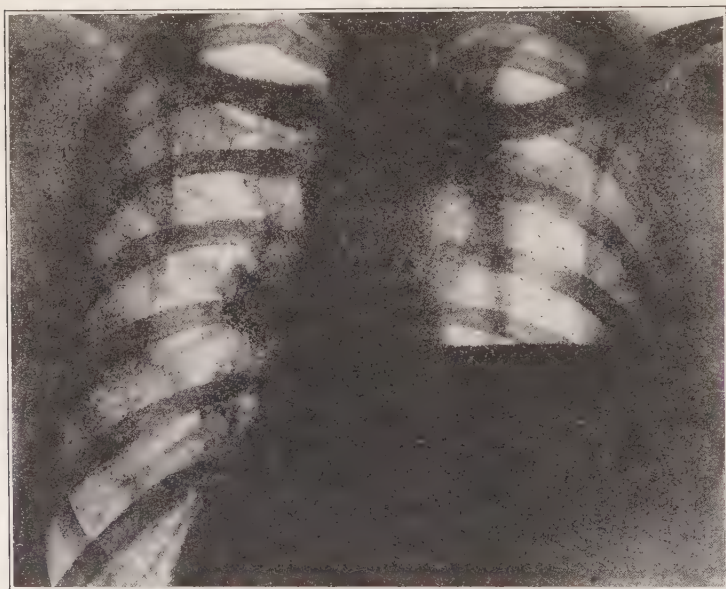
Gas Analysis.—In his experiments on dogs, Emerson found that if air be introduced into the chest there is an almost immediate accumulation of CO_2 and diminution of O in the pleura, but the N remains remarkably constant until a point is reached at which one may suppose that absorption is well under way, when the N rises about 8 per cent. and then remains quite constant. Analysis of the gas is of little assistance in judging the condition of the fistula, but an increasing amount of oxygen in portions of gas successively removed suggests an open fistula.

¹ Pneumothorax, Nouveau signe pathognomique de cette affection, *Gaz. f. hôp.*, April 4, 1857.

² *Montreal Med. Jour.*, 1895, 24, 969.

Air or gas which has gained entrance to the pleural cavity is absorbed, the rate of absorption varying with the condition of the pleura and the composition of the gas. Absorption is most rapid when the pleura is normal. According to Szupak's¹ investigations on dogs atmospheric air, O and CO₂ are absorbed at about the same rate, while N is taken up only about one-half as rapidly. In his review of clinical cases he finds that the time required for absorption in cases without friction rub or fluid exudate was from twenty-six days to two months. In one case the air was absorbed in six days and in another after three years. The possibility of slow leakage of air through the fistula or of inhibition from inflammation of the pleura are probably largely responsible for wide differences in the apparent rate of absorption.

FIG. 14



Pneumopyothorax of the right side. The fluid is indicated by the opaque shadow with horizontal upper border. Displacement of the heart to the left. The presence of air above the fluid is indicated by the clearness of the intercostal spaces and the absence of the normal lung markings. The collapsed lung is seen as a less dense, sharply outlined shadow with vertical margin above the fluid. (M. G. H. No. 188816.)

Roentgen-ray Examination.—This not only serves to confirm the results of physical examination but may show small collections of air not otherwise to be detected. Both the fluoroscope and the radiograph should be used. The position of the displaced heart, fracture of the ribs, and depression of the diaphragm may be noted. An accumulation of air is seen as an abnormally clear zone, over which the normal lung markings are absent and the ribs more sharply defined than at other parts of the chest. The collapsed lung is seen as a relatively dense, sharply limited, irregularly oval shadow in the mid-chest, in the region

¹ Experimentelle Untersuchungen über den Pneumothorax, Dorpat, 1891.

of the root of the lung. An incompletely retracted normal lung is less dense. Infiltration of the tissue may be responsible for failure to retract and may add to the density of the shadow. Adhesions may account for irregularities in the contour of the lung and appear as linear or band-like connections between the lung and the chest wall. Inspection of the other lung may disclose suggestive evidence of tuberculosis.

Pleural fluid appears as an opaque shadow at the bottom of the chest with its upper border constantly horizontal, independent of the patient's position. With the patient upright the upper border is transverse. When he lies on his side it is parallel to the long axis of the body. Examination with the fluoroscope shows a wavy motion of the surface on shaking the patient, tapping the abdomen with the fingers, percussion of the chest, or during cough. Still another motion is synchronous with cardiac systole, coincident with which very small waves start from the mediastinal region and travel across the surface to the chest wall.

Varieties.—Open Pneumothorax.—In this the mechanical relations are simple. An open fistula connects the pleura with the outside air and atmospheric pressure exists in the pleural space with respiratory oscillations about the zero point. If the fistula is wide open the collapsed lung takes little or no part in respiration and the intrapleural pressure remains nearly constant at zero. If the fistula is small the respiratory oscillations are greater and the pressure may become negative in inspiration and positive in expiration. To maintain its patency the fistula in the collapsed lung must usually be large, with rigid walls, and run in a direction perpendicular to the pulmonary surface; hence it is uncommon from perforation of the lung, but occurs more often in advanced pulmonary tuberculosis, occasionally in empyema rupturing through the bronchi, and may follow thoracotomy.

Respiratory embarrassment is due to collapse of the lung and displacement downward of the diaphragm and of the mediastinum to the sound side. Mediastinal displacement limits the excursion of the sound lung and the efficiency of respiration. Instability of the mediastinum aggravates the symptoms. If free to move, it is drawn toward the sound side during inspiration and moves toward the affected lung during expiration, in consequence of which a part of the expired air may be forced into the collapsed lung. During inspiration air is drawn not only from without into the trachea but also from the collapsed lung. The oscillation from one lung to the other of a volume of used air further reduces the efficiency of respiration. During forced expiration with cough, inflation of the collapsed lung is increased.

Valvular Pneumothorax.—This is the commonest form and is due to valve-like action of the fistula, which permits entrance of air into the pleura, but prevents its escape. Rupture of a small pulmonary cavity may connect the bronchi and pleura by way of a long, narrow, sinuous passage. Inspiration inflates the partially collapsed lung and draws air into the pleural cavity, but with the collapse of the lung during expiration the fistula is closed by apposition of its walls and the imprisoned air cannot escape. The deeper the inspiration the more air enters. Cough with closed glottis greatly increases intrapulmonary pressure, inflates the

collapsed lung, opens the fistula, and further distends the pleura. Tuberculosis is the cause in a large proportion of such cases.

The high degree of pressure which may be produced makes this form especially dangerous and encroachment on thoracic space and dislocation of the mediastinum may become extreme, with displacement of the heart, kinking of the great vessels, narrowing of the principal bronchi and diminished volume, elasticity and effectiveness of the sound lung. Mobility of the mediastinum increases the danger and thus the condition is more serious in young and healthy persons. The outcome depends on the behavior of the fistula. Total collapse of the lung favors healing of the fistula, but at times, after partial absorption of air and reinflation of the lung, the fistula again opens.

Pneumothorax Acutissimus.—This is also known as suffocative pneumothorax and the term is applied to cases in which death results within a few hours. A valvular fistula with the rapid development of a high positive pressure or grave complications in the lung or other organs may be responsible.

Closed Pneumothorax.—This is only a phase of the open or the valvular form and is favorable, since closure of the fistula is the necessary forerunner of recovery. The orifice of the fistula may be sealed by pleural inflammation or adhesion and union of the walls of the fistula. Collapse of the lung favors closure of the fistula and small perforating wounds or slight pulmonary lesions in a comparatively healthy lung may readily close in this way. This form is common in spontaneous pneumothorax, in relatively early tuberculous cases and after thoracentesis.

Double Pneumothorax.—This is uncommon. Death usually follows within a few hours. Life can be maintained only when the collapse of one or both lungs is incomplete. Hellin¹ collected a number of cases.

Partial Pneumothorax.—In this form adhesions limit the air to a circumscribed area. Any portion of the pleural sac may be the site. An apical localization may readily lead to confusion with a pulmonary cavity. In Monnier's² cases the pneumothorax was in the interlobar septum.

Recurrent Pneumothorax.—A number of instances of recurrent attacks of pneumothorax are recorded. In Sale's remarkable case³ there were 11 attacks within six years. Ljungdahl⁴ has reviewed the literature.

Artificial Pneumothorax.—In 1882, Forlanini⁵ suggested the possibility of treating pulmonary tuberculosis by establishing artificial pneumothorax on the affected side and in 1894 reported that he had used the method and described his technique. In 1898, Murphy⁶ reported 5 cases thus treated. Forlanini⁷ considered the method at length and reviewed the literature.

Theories.—The method is based on the assumption that, as for tuberculous processes elsewhere, immobilization is favorable for the arrest

¹ *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1909, vol. 17.

² *Gaz. méd. de Nantes*, November 2, 1907.

³ *Lancet*, 1907, i, 1572.

⁴ *Deutsch. Arch. f. klin. Med.*, 1918, vol. 126.

⁵ *Gaz. d. osp.*, 1882, vol. 3; *Gaz. med. di Torino*, 1894, vol. 65.

⁶ *Jour. Am. Med. Assn.*, 1908, 31, 151.

⁷ *Ergebn. d. inn. Med. u. d. Kinderh.*, 1912, 9, 621.

of a tuberculous process in the lung and may be secured by the insufflation of air or pure nitrogen into the pleural sac on the diseased side. Compression of the lung is an important factor, diminishing the size, evacuating the contents and approximating the walls of pulmonary cavities, lessening the amount of infectious material and thus retarding the activity of the tuberculous process.

Graham and Bell¹ conclude from experimental work that in its pressure relations the thorax is to be considered as one cavity and that any change of pressure in one pleural cavity will also affect the other almost equally. In cases in which the mediastinum is flexible, therefore, the objection that immobilization and compression of one lung must of necessity throw an added burden of work on the other is not well founded. The experimental studies of Simon² and Betchov³ are confirmatory of this conception.

Indications.—This method may be used in cases of pulmonary tuberculosis, after unsuccessful trial of other methods, and in unilateral cases with freedom of the pleura from adhesions. Some would include the predominantly unilateral cases with slight and relatively inactive processes in the opposite lung. The treatment is also recommended for intractable hemoptysis when its source from one or the other lung can be determined with tolerable certainty, and in pulmonary abscess developing in the central part of the lung and especially at the lung root without involvement of the pleura. Obliteration of the pleural sac, acute bilateral processes and grave cardiac or renal lesions are contraindications. Roentgen-ray examination is a necessary preliminary in the selection of cases.

Apparatus.—The apparatus used by Forlanini⁴ or its modifications by different workers⁵ consists of two glass receptacles connected by glass or rubber tubing. Atmospheric air is now generally used. Out of one receptacle air can be forced into the pleural sac by water or air pressure in the other, the water meanwhile acting as a seal to prevent the escape of air in other than the right direction. A manometer is so arranged that it can be brought into or out of connection with the system and the pleura. A special needle is used for the puncture. The air should be filtered through cotton on its way to the chest.

Methods.—In choosing the site for the injection, freedom from pleural adhesions is the most important determining factor and the injection is made wherever the pleura seems most likely to be free, although the lower parts of the chest least covered with muscular tissue are points of election. Freedom of the pleura from such a degree of adhesions as would be likely to prevent the production of pneumothorax is suggested by mobility of the pulmonary margin over a part or the whole of its

¹ *Am. Jour. Med. Sci.*, 1918, **156**, 839.

² *Am. Rev. Tuberc.*, 1921, **8**, 620.

³ *Schweiz. med. Wchnschr.*, 1921, **51**, 994.

⁴ *Apparate und Operationstechnik für den künstlichen Pneumothorax*, *Deutsch. med. Wchnschr.*, December 14 and 21, 1911. For detailed descriptions of the apparatus the reader is referred to the article quoted.

⁵ Robinson and Floyd: *Arch. Int. Med.*, 1912, **9**, 452. Balboni: *Med. Comm. Massachusetts Med. Soc.*, 1912, vol. **23**. Miller: *Jour. Am. Med. Assn.*, 1922, **78**, 425. Macmillan: *Ibid.*, 1922, **78**, 889. Singer: *Arch. of Surg.*, 1925, **10**, 312.

extent as determined by roentgen-ray examination, percussion of the complementary space during forced inspiration and expiration and observation of the diaphragm shadow. Diminution in amplitude or total absence of respiratory motion suggests partial or complete obliteration of the pleura, but may be due to such other causes as immobility of the lung from disease, weakness of the respiratory muscles, and increased intra-abdominal pressure. A history of pleurisy or lobar pneumonia on the affected side or pleural pain may suggest pleural adhesions.

Two methods are in use: in the Murphy-Brauer method, preceding the first injection an incision is made to the parietal pleura through which the needle is obliquely introduced, in that of Forlanini, thoracentesis is performed without preliminary incision. The incision method diminishes the danger of puncture of the lung and gas embolism, but is likely to result in a greater or less degree of subcutaneous emphysema. After the first injection it is customary to give subsequent treatment by the puncture method.

Preceding the puncture the skin should be frozen with ethyl chloride. The skin and underlying tissues are then anesthetized with 1 per cent. novocaine, containing 1 to 10,000 epinephrine. The needle, unconnected with the apparatus and with the stopcock on the lateral outlet closed, is introduced to what seems a proper depth, the trocar is removed, and the needle-cock closed. The needle is now connected with the manometer of the apparatus, the air system meanwhile remaining closed. The position of the point of the needle just within the two layers of the pleura is indicated by the appearance of *negative pressure and marked respiratory oscillations* in the manometer, in the absence of which it is never safe to proceed with the injection, which must be abandoned or another site chosen. If the point of the needle is in the thoracic wall, in a bloodvessel or in adherent pleura, negative pressure and respiratory oscillations are absent, if in the lung, respiratory oscillations may be present but there will be no constant negative pressure. If the point of the needle lies in the endothoracic fascia, *slight* negative pressure and respiratory oscillations may be present. Aspiration by a syringe attached to the needle may help to exclude the possibility of puncture of a vein.

If the desired negative pressure and respiratory oscillations are obtained, the manometer is excluded and the air system brought into connection with the needle, through which air is allowed to flow into the pleural sac under very slight pressure, to an amount varying usually from 50 to 500 cc. Small amounts are reinjected at intervals, commonly at first each week. The amount and frequency are determined by the conditions in individual cases, the indication being to maintain the affected lung completely immobile. Distress or pain during the injection indicates a dangerous degree of tension on adhesions and makes it wise to terminate the procedure.

Dangers.—Embolism is the most immediate danger and when it occurs is commonly fatal if large amounts of gas have entered a vein. Of 98 cases treated by Forlanini, this accident occurred with a fatal result in 2 during a repetition of the injection. Sercer and Peicic¹ col-

¹ *Beiträg. z. Klin. d. Tuberk.*, 1922, **53**, 123.

lected 17 published cases in which gas embolism caused a fatal termination. Death apparently due to "deep emphysema" has been observed in 3 instances. Hemiplegia has followed. Sudden death apparently due to irritation of the pleura ("eclampsic pleurisy") is occasionally observed, but may follow puncture of the pleura for any reason. Thorough local anesthesia previous to the injection will probably largely prevent it. Infection may follow the introduction of organisms from within or without. It has been estimated that an exudate complicates about one-half the cases. Weiss¹ was always able to demonstrate tubercle bacilli in the effusion by animal inoculation. Such an extension of the tuberculous process cannot be regarded as desirable.

The effect of maintaining the lung in a collapsed condition for a long period is an important consideration. In collapse of the lung in consequence of pleurisy with effusion, the formation of extensive pleural adhesions and of dense connective tissue on the surface and within the substance of the lung may develop in the course of time and prevent reëxpansion. Such indurative changes are more common with empyema than with serofibrinous effusions and are more pronounced the longer the lung is allowed to remain in a contracted and atelectatic condition. They constitute an important argument for the early removal of inflammatory and especially purulent fluid. Similar changes in the pleura and lung have been observed as a complication of artificial pneumothorax. Graetz² demonstrated dense fibrous thickening of the pleura over the collapsed lung. Bruns³ found thickening of the pulmonary pleura and an increase in the peribronchial and perivascular connective tissue after experimental pneumothorax in animals. Kaufmann's⁴ findings are still further confirmatory. He found the lung incapable of reëxpansion in consequence of such changes. Pulmonary collapse is likely to be more complete in those parts of the lung which are little or not at all involved.

Emphysema of greater or less extent is common after the Murphy-Brauer incision method but is more annoying than dangerous. It was observed in 60 per cent. of Robinson and Floyd's cases. It is less frequent when Forlanini's puncture method is used. The rapid evacuation of the contents of tuberculous cavities under compression may lead to further infection in near-by or remote parts of the lung. Dyspnoea and collapse from displacement of the mediastinum and heart, pain from the stretching of adhesions and gastric symptoms from displacement downward of the diaphragm may follow.

Results.—Among the more immediate effects are diminution of fever and disappearance of night-sweats, ascribed to diminished absorption of toxic material. The amount of sputum may at first increase, with later diminution in the cough and expectoration.

Sufficient time has elapsed for the collection of statistics on the late results and the literature contains many favorable reports on small groups

¹ *Beiträg. z. Klin. d. Tuberk.*, 1912, **24**, 333.

² *Ibid.*, 1908, **10**, 249.

³ *Ibid.*, 1909, **12**, 1.

⁴ Ueber die Verhanderung d. Pleura u. Lungen gesunder Hunde mit künstlichen Pneumothorax, *Ibid.*, 1912, **23**, 57.

of cases but for the most part a strictly comparable control group is lacking. Comparison of the results obtained in lung collapse cases and that in cases otherwise similar but not so treated is made by Saugmann¹ and by Matson, Matson and Bisaillon.² Of 218 treated cases in Saugmann's series, 130 (59.3 per cent.) died of tuberculosis. Of 92 untreated cases, 79 (85.9 per cent.) died from the same cause. Of 600 cases in Matson, Matson and Bisaillon's series, among 235 in whom a satisfactory collapse was obtained, 52 (22 per cent.) died, while of 245 with a partial collapse, 142 (58 per cent.) succumbed and of 120 in whom the attempt to produce artificial pneumothorax was unsuccessful 80 (66 per cent.) died.

Diagnosis.—When in the course of chronic pulmonary tuberculosis there is sudden pain in the side, immediately followed by severe dyspnoea, pneumothorax should be suspected. *Resonance on percussion with suppression or absence of the respiratory murmur* often gives the first intimation of the nature of the trouble. Displacement of the heart away from the affected side is confirmatory and the diagnosis may be regarded as established if the succussion splash of pleural fluid is heard. Other signs of importance are diminished or absent tactile fremitus, voice sounds and whisper, the amphoric phenomena, metallic tinkle, coin sound, and movable dulness at the base with horizontal upper border irrespective of the position of the patient. The auscultatory phenomena are essential for the diagnosis. With mild symptoms and a small pneumothorax, especially if uncomplicated by fluid, the diagnosis is difficult and the condition is usually overlooked. Examination by the roentgen-rays may make a diagnosis possible when other means fail.

There may be difficulty in differentiating pneumothorax from the following conditions:

A *large pulmonary cavity* may show resonance or tympany on percussion, cracked-pot sound, changes in the percussion note with the mouth open or closed, on changing the position of the patient and during inspiration or expiration. If the cavity is large and contains thin fluid, there may be movable dulness with horizontal upper border below the resonant area. Amphoric breathing, metallic tinkle, the coin sound and succussion splash may also be present. With cavity, however, the symptoms are likely to be gradually progressive, without a history of sudden pain and severe dyspnoea. With cavity the affected side is likely to be retracted and the intercostal spaces narrowed. The upper lobes or the apex are likely to be affected over a less extensive and more definitely circumscribed area over which there is loud bronchial breathing, increase of voice, whisper and tactile fremitus and abundant rales. The heart is drawn toward the affected side and the diaphragm elevated rather than depressed. In cases in which there is a large loss of pulmonary substance involving the greater part or the whole of one lung the differentiation may be difficult. Examination by the roentgen-rays may be of assistance. The absence of the shadow of the retracted lung at the root and the presence of a shadow with a central clear area are suggestive of cavity.

¹ *Ztschr. f. Tuberk.*, 1921, vol. 34.

² *Am. Rev. Tuberc.*, 1924, 9, abstracts, 23.

In the presence of *bronchostenosis*, the signs over the parts of the lung supplied by the occluded passage may simulate those due to pneumothorax. If the obstruction is valve-like and causes acute pulmonary inflation with displacement of the heart away from the affected side the condition is still more suggestive of pneumothorax. Confusion with pneumothorax of lung changes secondary to bronchostenosis may be avoided by roentgen-ray examination.

Subphrenic pyopneumothorax, first accurately described by Leyden,¹ may offer great difficulty. A collection of air and pus is present between the diaphragm and the liver or between the diaphragm and the spleen, stomach and colon. Perforation of a gastric or duodenal ulcer or the appendix are the usual causes, but in rare instances gas may be formed by the colon bacillus and without evidence of perforation of the intestine. The diaphragm may be elevated as far as the third or even the second rib with displacement downward of the liver and other abdominal organs. Over the cavity containing air and fluid, occupying the lower part of the chest, there are physical signs of pyopneumothorax. There may be resonance or tympany on percussion above, movable dullness below, diminished and anphoric or absent respiratory murmur, vocal and tactile fremitus and whisper and metallic tinkle, coin sound, and succussion splash. Absence of cough and expectoration and a history of preceding abdominal symptoms may suggest an abdominal origin, the heart is only slightly displaced, the intercostal spaces may show inspiratory depression, the vesicular breathing terminates abruptly where the signs of pyopneumothorax begin and respiratory mobility of the pulmonary margin may be determined. Foul pus with a fecal odor may be demonstrated by exploratory puncture and an increase in the tension during inspiration and decrease during expiration may be determined. Examination with the roentgen-rays may furnish important evidence. In cases in which the pyopneumothorax is circumscribed and the upward dislocation involves only a part of the diaphragm, an abrupt dome-like elevation of the shadow may be noted, with evidence of air above and fluid below. With larger accumulations the diaphragm may be elevated as a whole although still maintaining its oval contour with persistence of a relatively clear space in the costo-phrenic sinus. If pleurisy with effusion complicates the process, the roentgen-ray picture is obscured. On examination with the fluoroscope inspiratory depression and expiratory elevation of the diaphragm may be seen and the diaphragmatic excursion is usually greater than with pneumothorax.

Eventration of the diaphragm may be a cause of confusion but is rare. Bayne-Jones³ reported 45 cases in 1916. Jaffin and Honeij² observed an instance in 1923. One case has come under my observation. The left diaphragm is usually involved. The heart and mediastinum are displaced to the right and there is dullness, diminished or absent breathing, voice, whisper and tactile fremitus below the level of the elevated diaphragm. There may be tympany and succussion. The signs vary with the amount

¹ *Ztschr. f. klin. Med.*, 1880, vol. 1; *Berl. klin. Wchschr.*, 1892, vol. 46.

² *Arch. Int. Med.*, 1916, 17, 221.

³ *Boston Med. and Surg. Jour.*, 1923, 188, 593.

of fluid and air in the stomach and change on shifting the position of the patient. The condition is most likely to be mistaken for air and fluid in the pleural cavity from which it may be distinguished by the absence of the usual symptoms accompanying pneumothorax, variation in physical signs according to the contents of the stomach, less displacement of the heart than would be expected from air and fluid of equal amount in the pleural cavity and by roentgen-ray examination. Exploratory puncture is dangerous in eventration of the diaphragm and in doubtful cases should be postponed until after roentgen-ray examination.

Diaphragmatic hernia is likely to be a cause of confusion only in the uncommon instances in which there is considerable encroachment on pulmonary space by the passage of the abdominal contents through the hernial opening. Grosser¹ reviewed the reported instances which up to that time comprised for the most part autopsy cases. The diagnosis was seldom made during life before roentgen-ray examination of the gastro-intestinal tract became a common practice; and Henry I. Bowditch's clinical diagnosis,² confirmed by autopsy, in 1846 is noteworthy. Fineman and Connor³ estimate its occurrence at 1 in 23,000 cases at the Mayo Clinic. There are 7 instances in my series (5 M. G. H. and 2 private cases).

Diaphragmatic hernia may in rare instances be congenital but is more commonly acquired as the result of stab or gunshot wounds, a fall, contusion or concussion. The left side is usually involved and the stomach protrudes into the chest. With a large defect in the diaphragm the transverse colon, the omentum, small intestine, and even the liver or spleen may be contained in the sac. In common with pneumohydrothorax, there may be enlargement of the side, diminished respiratory excursion, diminished amplitude or absence of the diaphragm shadow, immobility of the pulmonary margin as determined by percussion, dislocation of the heart and mediastinum, tympany on percussion above with dulness shifting with change of position below, coin sound, diminished respiratory murmur, voice sounds and tactile fremitus and succussion splash. On examination with the roentgen-rays, an area suggesting air above and fluid below may be seen (Fig. 15) and, as in pneumohydrothorax, the fluid may be seen to maintain a horizontal upper border on changing the position of the patient. Waves of surface motion also may be observed during respiration and with cardiac systole.

A history of trauma, such gastro-intestinal symptoms as pain, attacks of colic, nausea, and vomiting and, in rare instances, hematemesis and the absence of cough and expectoration may call attention to the abdomen as a source of the disturbance. In one of my cases (Fig. 15), a man, aged twenty-four years, there was dyspnoea from early youth and inability to lie on the back without cough and choking sensation. Changes in the physical signs dependent on a full or empty stomach, sounds over the chest resembling the movement of flatus in the intestine and the absence

¹ *Wien. klin. Wchnschr.*, 1899, p. 655.

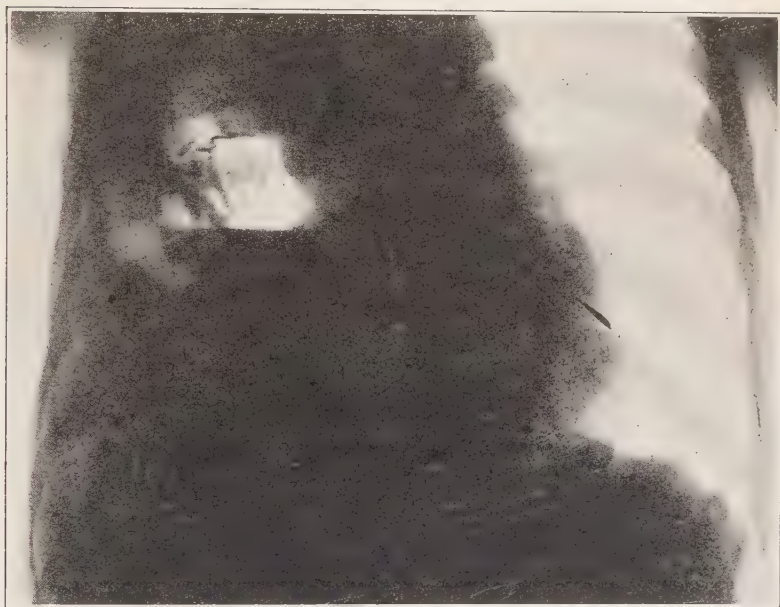
² *A Treatise on Diaphragmatic Hernia*, Jewett Thomas Company, Buffalo, 1853.

³ *Am. Jour. Med. Sci.*, 1924, **167**, 672.

of stomach tympany at its normal position after inflation with gas may serve to suggest the diagnosis. The roentgen-ray examination may show inspiratory depression and expiratory elevation of the fluid (unlike the paradoxical mobility in pneumohydrothorax) and after a bismuth meal the position and outline of the stomach or intestines in the thorax.

In *pneumonia* over and beside the consolidated area and in *pleurisy with effusion* over the collapsed lung, the percussion note may have a tympanitic and metallic quality, and amphoric auscultatory phenomena may be present, but in the former the history and clinical course and in both the increase of voice, whisper and tactile fremitus, and the absence

FIG. 15



Diaphragmatic hernia. Barium was seen by fluoroscope to pass through the œsophagus into the stomach in the usual manner and then upward to fill the bright area in the left chest. Outline of the stomach on the left side with masses of barium clinging to the gastric wall above and fluid level below. Remainder of left lung field dense. Below are shadows of barium in colon following barium enema. Displacement of heart to right. (Male, aged twenty-four years. M. G. H. No. 255012. March 9, 1923. Dextrocardia discovered in 1905 and chest condition then interpreted as hydropneumothorax. Death from tuberculous peritonitis, March, 1923.)

of metallic tinkle, coin-sound and succussion splash and movable dullness with horizontal upper border usually serve to make the differentiation.

Recognition of the *type* of pneumothorax is not always easy nor is it usually of practical importance. In the valvular form the dyspnœa is likely to be severe and persistent or gradually increasing with distention of the side and marked dislocation of the heart, mediastinum, and diaphragm. Intrapleural tension is likely to be persistently positive. With open pneumothorax, the dyspnœa, distention of the side, and dislocation

of organs are less marked. Changes in the percussion note with the mouth open and closed are more likely to be present. Intrapleural tension is that of the atmosphere with respiratory oscillations about the zero point and there is a rapid return to atmospheric pressure after aspiration. A gas analysis which shows 5 per cent., or less of CO_2 or a persistent increase in O in successive portions removed suggests an open fistula. When the pneumothorax becomes closed the dyspnoea diminishes, displaced organs return, positive pressure may persist at the height of inspiration and gas analysis may show a large percentage of CO_2 . The determination of the cause is important. A history of preceding hemoptysis out of a clear sky or a primary pleurisy, cough for several months, night-sweats, fever and failing weight and strength usually indicate tuberculosis, which owing to the compression of the lung often can be established by the finding of tubercle bacilli in the expectoration. The fact that from 80 to 90 per cent. of all cases are of tuberculous origin may well influence a decision in doubtful cases, and all cases should be regarded as tuberculous until proved otherwise.

Course and Prognosis.—This depends for the most part on the underlying disease. The pneumothorax is of itself usually of relatively little importance, as the patient soon develops a tolerance of the condition. Air alone does not irritate the pleura and is usually absorbed in the course of from one to two months.

As a complication of pulmonary tuberculosis, it introduces very definite dangers and hastens the fatal termination. The rupture of a small subpleural tubercle, a tuberculous cavity or a pleural adhesion usually leads to tuberculous or pyogenic infection of the pleura, with the formation of a serofibrinous or purulent effusion, in consequence of which the fever becomes more marked and emaciation progresses more rapidly. West¹ finds the mortality highest in the first few days, 10 of 39 cases dying on the first day, 18 during the first week. Among 74 cases, 45 died in the first month. The general mortality was about 70 per cent. Among Drasche's 198 cases, 71 per cent. died within the first fourteen days. Death may be ascribed to suffocation from the pneumothorax itself or flooding of the opposite lung with pus, to rapid extension of tuberculous or septic material into the pleura or to the original disease, phthisis. Hughes' remarkable patient lived at least three years and two months after the occurrence of pneumothorax, was able to attend his regular business and amused his friends by the succussion sound. In the case reported by Magnus-Levy² a pneumothorax was known to have lasted for at least eight and perhaps for twenty years. Gas analysis showed 5.5 per cent. carbonic acid and 12 to 23 per cent. oxygen suggesting a relatively wide communication between the pleural cavity and the air passages. In a small proportion of the cases an effusion fails to develop, or if present is absorbed or successfully evacuated and the patient's recovery is permanent and complete.

¹ *Lancet*, 1897, i, 1264.

² *Deutsch. med. Wchnschr.*, 1918, 44, 757.

Spengler¹ reported 10 cases of tuberculous pneumothorax with recovery and in 6 there was simultaneous arrest of the pulmonary tuberculosis. To the time of his report a total of 38 cases of healed tuberculous pneumothorax could be found in the literature. West estimates complete recovery at not over 10 per cent. and this may be regarded as a conservative estimate.

The prognosis of the spontaneous cases, unless of the suffocative type, is favorable, only 1 death occurring in 58 cases studied by Fussell and Riesman. In one of my cases of spontaneous pneumothorax the condition persisted for sixteen months and was followed by complete recovery. Uncomplicated traumatic cases usually also do well. Suffocative pneumothorax is rapidly fatal unless relieved by operation.

Treatment.—The indications are, on the one hand, to promote closure of the pulmonary fistula and prevent infection of the pleura and on the other to relieve a dangerous degree of embarrassment to respiration and the unfavorable consequences of pleural effusion more especially of the purulent form. Inasmuch as removal of air or fluid by decreasing intrapleural tension tends to reinflate the collapsed lung, reopen a pulmonary fistula and aspirate infectious material from the lung or bronchi into the pleura the indications are mutually conflicting and a conservative middle course is often the wisest plan.

In ordinary and other than urgent cases immediately following the rupture the patient should be absolutely at rest in bed. Irritative and unproductive cough should so far as possible be suppressed and deep respiration avoided in order to hasten closure of the fistula and prevent further entrance of air into the pleura. Strapping the affected side with adhesive plaster may help and morphine may be of assistance in quieting cough. In mild and moderately severe cases no further treatment is usually needed. The patient should be absolutely quiet for two or three weeks or until there is reason to believe that the fistula is closed. Traumatic and spontaneous cases usually do well under such conservative management.

In cases in which the pneumothorax rapidly increases, with urgent dyspnoea, cyanosis and great displacement of the heart, immediate relief must be offered. Pneumothorax acutissimus and certain cases of the valvular form are of this type. Puncture may prove life-saving, but aspiration should be avoided for fear of reopening the fistula. With valvular pneumothorax the pleural sac is likely to be reinflated and the puncture may need to be repeated or the cannula left in place for a time. Infection through the chest wall is to be avoided by the strictest asepsis. Thoracotomy with insertion of a drainage tube, converting the valvular into open pneumothorax with external fistula, is occasionally necessary.

With hemopneumothorax and hydropneumothorax with a small or moderate amount of fluid and without pressure symptoms, it is best to leave the fluid undisturbed for at least two or three weeks or until closure of the fistula is established. With large fluid accumulations or with pressure symptoms it may be necessary to tap, but it is best to withdraw

¹ *Beiträg. z. klin. Chir.*, 1906, **44**, 68.

only small amounts at frequent intervals and without forcible aspiration. The indications are essentially those with uncomplicated serofibrinous effusions with the exception that here the danger incident to the fluid must be weighed against that of opening the fistula, and the latter justifies a delay in doubtful cases.

With seropurulent and sterile purulent effusions in which symptoms of sepsis are absent or slight, it is best if possible to wait until the fistula is closed. If removal is indicated simple aspiration and the repeated removal of from 500 to 700 cc. may suffice. With frankly purulent fluid containing pyogenic organisms and with marked symptoms of sepsis, further regard for the fistula must be abandoned and free drainage established as for ordinary empyema. With putrid exudates an immediate operation is demanded.

CHAPTER X

DISEASES OF THE MEDIASTINUM

By HENRY A. CHRISTIAN, A.M., M.D., LL.D.

Introduction.—As ordinarily used, the term diseases of the mediastinum is purely a conventional one. It does not comprise all diseased conditions of the organs situated in the mediastinum, but only such as are not conveniently grouped under other headings. Under diseases of the mediastinum it is convenient to consider neoplastic and inflammatory conditions which originate in or chiefly affect the mediastinum. Almost all of the conditions to be described have their main seat in the superior mediastinum, that part above the upper border of the heart; it may be convenient at times further to divide this into an anterior and posterior part by a plane passing laterally through the trachea, but a strict anatomical subdivision will not add to the clearness of the subject. Rather it is the purpose to consider the mediastinum as a whole and to discuss the effect of diseased conditions on its contents, with only occasional reference to an anterior and a posterior, a superior and an inferior mediastinum.

TUMORS OF THE MEDIASTINUM

Of diseases of the mediastinum tumors form the group of greatest interest and importance. Both primary and secondary tumors occur in the mediastinum. *Primary* tumors may take their origin from any of the structures in this region, but probably their most frequent origin is in the mediastinal lymph nodes and thymus. *Secondary* tumors enter the mediastinum either by metastasis or by direct extension. They are usually small and of themselves clinically unimportant. If large, they produce symptoms and physical signs like those of a primary tumor.

In the mediastinum with its complex content a variety of primary tumors may develop. Fibroma, lipoma, chondroma, osteochondroma, myoma, lymphoma or lympho-sarcoma, including the tumor masses of Hodgkin's disease, sarcoma, endothelioma, carcinoma, simple cyst, dermoid cyst, and teratoma occur; of these the lymphoma group occurs most frequently. All of these, except lymphoma, sarcoma, carcinoma and rarely teratoma, are benign, in the sense that they do not invade or metastasize. However, since the mediastinum is a confined space of small dimensions, containing many important structures, any one of these in its growth may produce serious pressure symptoms, and tumors, which in other parts of the body are of little moment, may prove fatal here, even before attaining any very great size.

Simple Benign Tumors.—Simple benign tumors, such as fibroma, lipoma, chondroma, and myoma, are of very infrequent occurrence in

the mediastinum, and often are accidental postmortem findings. Cases which, during life, have shown symptoms due to their presence, are as yet too few to justify any attempt to construct a special symptomatology. It is sufficient to bear them in mind in connection with patients showing slight or long-continued signs of mediastinal tumor. Though benign, they may, however, cause serious disturbance from pressure on adjacent structures. Their benign nature may not be recognized during life. If diagnosed, there is a good chance of successful surgical removal. This group is well illustrated by two patients observed at the Peter Bent Brigham Hospital.

J. H. P., Med. No. 8219, male, aged thirty-five years, was admitted to the Peter Bent Brigham Hospital March 4, 1918, complaining of pain in the chest. In 1905 the patient was struck in the chest by the knee of a horse while trying to stop a runaway. For two to three days after this, his chest was sore but he had no other symptoms. Three years later he began to have a dull pain in the region of the left nipple which was brought on by work in which he had to extend his arms above his head. This pain would persist at times for a few hours only and at other times would last throughout the day. At first it came about once a week. Otherwise his general health was excellent and he had no other symptoms. Three years later, in addition to the pain already described, there developed a prickling sensation in the region of the left nipple which came on at first only at night. None of these disturbances was severe enough to keep him awake. A year later he commenced to have a sharp stabbing sensation in these same areas which would come on a half dozen times during the day and last a few seconds. This was severe enough to cause him to stop if he was at work, but if he was walking it did not compel him to stand still. Occasionally this pain kept him awake at night. During the three months before admission these symptoms became worse and in addition he had tingling in the upper part of his left arm running down to the little finger, and a slight cough.

Physical examination was negative except for a distinctly rounded, slight protuberance just to the left of the sternum in the second and third interspaces over which there was a slightly heaving impulse, synchronous with the heart, accompanied by a slight thrill and slight systolic bruit. On percussion there was slight dullness over this area, which extended a little beyond the visible prominence. Roentgen-ray examination showed in this region, extending out to 2 cm. from the arch of the aorta, a distinct shadow with a very smooth, rounded contour, distinctly less dense than the heart and aorta but slightly denser than the ordinary pulmonary density. On lateral view this was seen to be immediately in contact with the anterior chest wall and in stereoscopic plates it could be seen to overlies the arch of the aorta. It was thought at first to be a cyst and it seemed easily accessible for surgical removal. Dr. David Cheever removed a roughly spherical tumor mass, $3\frac{1}{2} \times 5 \times 6$ cm., which was easily enucleated, apparently not being intimately attached to any of the surrounding structures. It proved to be a rather oedematous fibrous tumor which gave the histological structure of neurofibroma. The patient made a complete recovery and six years later is free from all symptoms of the tumor.

F. A. L., Med. No. 3333, male, aged fifty-one years, was admitted to the Peter Bent Brigham Hospital September 14, 1915, complaining of cough and dyspnoea. His cough began about a year prior to this date during the summer time and became much worse during the autumn. The cough was particularly bad at night, though it occurred in the day. It was brassy in character but only in the morning did he raise any sputum. The cough had progressively grown worse until just before admission it was preventing his sleeping almost entirely. Physical examination was essentially negative except for a few rales in his lung. After a test meal the Rehfuß tube seemed to be withdrawn with some difficulty as if it were caught in a spasmodic contraction of the œsophagus. A roentgen-ray showed a normal heart shadow with a definite shadow extending a considerable distance to the left beyond the normal shadow of the left auricle. This seemed to pulsate corresponding to the diastole of the ventricle when observed under the fluoroscope. A month later fluoroscopic examination showed the same thing and his symptoms persisted. In February, 1916, he had an ischiorectal abscess accompanied by a severe bronchitis with fever. There were many moist rales over the bases of both lungs, more on the left side. The sputum increased so that it averaged about 150 cc. per day. He was dyspnoeic after exertion, his cough was severe, he had occasional sweating and some elevation of temperature. Fluoroscopic examination showed an increased size of the shadow. A little later he developed an infection of his cheek and died, apparently from septicemia, on May 10, 1916. Autopsy showed a tumor in the anterior mediastinal space above the pericardium which was flat, oval, of rather firm consistency, and measured 9 x 8 x 4 cm. It was attached to the anterior wall of the pericardium. On section it was composed of numerous lobes of grayish color, separated from one another by bands of firmer connective tissue. Histologically it was composed of masses of connective tissue cells, irregularly arranged, the individual cells, spindle in shape, with fusiform nuclei, rich in chromatin. Fibrous-tissue fibrils were abundant. The pathological diagnosis was fibroma durum.

In contrast to the simple benign tumors are the malignant ones. These are not excessively rare, but form a fairly definite though small proportion of hospital medical cases (1 to 500 at St. Bartholomew's Hospital, London). Furthermore, their clinical course and physical signs are sufficiently characteristic to lead to a correct diagnosis in the larger percentage of the cases.

Lymphoma or Lymphosarcoma.—These, of all tumors of the mediastinum, are the most frequent, although in the older books carcinoma is given as the most common primary tumor. This, however, is undoubtedly due to errors in terminology and diagnosis. Hare, in whose collection of 520 cases of mediastinal disease 98 are given as sarcoma and 134 as cancer, merely classifies them according to the author's diagnosis, without any criticism of its correctness, and does not exclude secondary tumors. This apparent frequency of cancer is due to the earlier use of this word for any cellular malignant tumor, shown by the fact that the larger number of Hare's cases of cancer antedate 1880, while the reverse is true of sarcoma. The very great preponderance of lymphoma over carcinoma in the

recent literature shows the comparative infrequency of the latter. At present, classifying tumors on a structural basis, we reserve the terms carcinoma and cancer for tumors clearly epithelial in structure and cell grouping. Such are undoubtedly infrequent in the mediastinum, while tumors structurally of the lymphoma group are relatively frequent.

Lymphosarcoma can originate in the peribronchial and mediastinal lymph nodes and in the thymus. It is not possible to determine which of these is the most common point of origin, since in few cases at autopsy are the relations or the structure such as to definitely reveal the beginning point of the tumor.

Under the term lymphoma or lymphosarcoma we include a group of tumors of a general type, with extremes of cells and intercellular substance. To them a variety of names have been given, lymphoma, malignant lymphoma, lymphocytoma, round-cell sarcoma, lymphadenoma, etc., and the attempt has been made to distinguish different varieties and to separate them into benign and malignant tumors. Here, too, can be properly grouped the mediastinal masses of Hodgkin's disease.

The lymphosarcomata are usually lobulate, consisting of tumor masses separated by a varying amount of connective tissue. The tumor masses may be soft and very cellular or dense and quite fibrous. Usually they are grayish or pinkish-gray in color. Sometimes they show yellowish areas of necrosis. Calcification is extremely rare and hemorrhage is uncommon. They compress and surround adjacent structures but it is unusual for them to invade or to metastasize except into adjacent lymphoid structures. Occasionally, however, they do invade or metastasize.

These tumors are not uncommon in the first decade and have been reported soon after birth. In the decades between ten and sixty the regularity of distribution is very noticeable. There seems to be no age at which they are particularly common and none at which they may not occur. Males slightly preponderate.

Symptoms.—The character of the symptoms in lymphoma or lymphosarcoma of the mediastinum varies much in individual cases. However, two general types occur: (1) Cases of gradual onset and progressive development of symptoms; and (2) cases with a sudden appearance of symptoms and a rapid subsequent course. The former is the more usual. Ordinarily the patients give a history of an increasing shortness of breath, particularly following moderate exertion or there is a persistent cough. Very frequently both are present, and combined with them is a sense of fulness, with feeling of oppression in the chest, with or without moderate pain. Such symptoms gradually increase in severity, and within a few months cause the patient to consult a physician for dyspnoea or for the discomfort or pain in the chest. Not infrequently a pleural effusion is the first indication of the disease.

With the other group there are, as it were, no premonitory symptoms. Dyspnoea appears quite suddenly or there may be an attack of suffocation. Sometimes a severe cough or pain in the chest is the first warning. These cases may become quiescent and remain so for some length of time, but this is rare, as the average duration of lymphosarcoma in this region is less than one year.

There are many variations from these types. Symptoms are almost entirely the result of pressure; what they are depends on the structures pressed upon and the degree of the pressure. One tumor, while still small, encroaches on some important mediastinal structure with resultant early definite symptoms; another grows to considerable size before any structure is functionally involved, and symptoms appear slowly. It is surprising how large a mediastinal tumor may be at the time it causes the first symptom.

The most common symptom is *dyspnœa*. Rarely is this absent; ordinarily it is early and almost every patient at some time during the course is dyspnœic. It may be the result of pressure on the heart or lungs, obstruction of the trachea or bronchi, chronic passive congestion of the lungs, or irritation or destruction of the recurrent laryngeal nerve, and these causes may act singly or in combination. In most cases it occurs in the form of recurrent attacks, at first only after physical exertion or emotion. Gradually the attacks become more and more frequent and less dependent on exciting causes. Finally, dyspnœa becomes practically continuous. Respiratory rhythm in proportion to the dyspnœa is usually slow. The dyspnœa is either inspiratory, or both inspiratory and expiratory. It may be accompanied by stridor. In the later stages the patient is prevented from assuming a recumbent posture and sleep is more and more interfered with. In not a few cases death results from suffocation, and, in almost all, dyspnœa contributes largely to the lethal outcome.

Pain is frequent, particularly in the later stages, often severe, but in most cases not excessive. At first there is usually only a sense of weight and oppression in the chest; later, more definite pain. Not infrequently moderate paroxysms of pain occur which radiate up the neck or down the arm. There may be localized numbness or pain in one arm, the result of pressure on the brachial plexus or its roots. More rarely there is intercostal pain due to pressure on the intercostal nerve roots near their exit from the spinal column. A number of cases run an almost painless course and the constant, intense, boring pain which characterizes many aneurisms is quite exceptional.

Cough is common and may result from vagus irritation, but more often is the result of bronchitis associated with pressure on the respiratory tract. In some cases cough is a dominant feature, persistent and difficult to control. Often there are paroxysms separated by varying periods of freedom. In a number of cases cough has been slight or even absent. With the cough there is practically always a mucous or mucopurulent expectoration, often very copious. At times pressure on a bronchus leads to bronchiectasis with its characteristic sputum, abundant, separating into three layers on standing and foul of odor. Frequently the sputum is blood-streaked and in a few cases there is hemoptysis suggestive of pulmonary tuberculosis. Examination of the sputum yields no positive diagnostic evidence.

Dysphagia occurs in some cases, but is not very common as an early symptom, since the œsophagus, by its position and structure, is well guarded from obstruction due to mediastinal neoplasms.

Hoarseness and a weak voice are common later symptoms and there may be aphonia. These result from pressure on the recurrent laryngeal nerve but it should be borne in mind that paralyses of the vocal cords may be present without change of voice and remain undetected unless the larynx is examined,

With these symptoms there may be a loss of appetite, progressive muscular weakness, and a decrease of subcutaneous fat, all signs of a serious progressing malady. The course is, in most cases, relatively a rapid one. Without roentgen-ray treatment death ensues usually in about six months after the development of definite symptoms and not many live longer than one year. Slowly growing, more fibrous tumors extend over a longer period, but they are not the more common form. On the other hand the course may be fulminant, as the one reported by Jaccoud with death in eight days after the first symptom.

Physical Signs.—Inspection may yield much diagnostic information. A *deformity of the upper anterior thorax*, consisting of a median or medio-lateral bulging of the chest wall, may be evident. In other cases no deformity of the bony wall of the thorax exists, but a slight fulness of the intercostal spaces adjacent to the sternum may be noted. Accompanying a prominence of the chest wall, or independent of deformity, a localized pulsation may be seen. This is much more characteristic of aneurism, but may occur in mediastinal tumor, either as a transmitted aortic pulsation, the pulsation of a vein distended from obstruction, or the pulsation of an extremely vascular tumor. The latter may be even expansile in character and closely simulate an aneurismal pulsation; however, a systolic bruit heard over such an area is extraordinarily rare in tumor, while common in aneurism. An aortic diastolic murmur if present makes aneurism almost a certainty.

In a large percentage of cases, particularly in the later stages, a *dilatation of the superficial veins* of the thorax and neck is apparent, and this is more apt to be unilateral than bilateral. Not infrequently the jugular veins stand out as prominent cords, or tortuous veins of considerable diameter may be seen coursing over the anterior chest. Sometimes these vessels are limited in distribution to the chest wall in front, between the clavicle and third or fourth ribs. In other cases they may extend down to or even below the level of the attachment of the diaphragm, appear in the back, and extend up along the neck or to the face. With involvement of the veins of the neck and face *exophthalmos* may be produced. Similarly the veins of the arm may be distended and tortuous.

Localized cyanosis is not uncommon, accompanying the venous dilatation and corresponding to the distribution of the dilated veins, although it may occur without venous dilatation. In other cases cyanosis is more general, being due to interference with normal respiration or the result of defective cardiac action. In these cases the cyanosis is like that common in cardiac and respiratory disease.

Rather more striking than cyanosis is *localized subcutaneous œdema* with or without prominent superficial veins. The distribution of this varies in individual cases as does that of the dilated veins. Localized venous dilatations, cyanosis and œdema result from pressure on veins,

more commonly pressure on the superior vena cava or some of its larger branches. As the obstruction increases, collateral circulation takes place by way of the internal mammary, the intercostal and the azygos veins. In some cases this collateral circulation is sufficient to prevent signs of venous obstruction. The superior vena cava is rarely obstructed near enough the heart to occlude the azygos vein. In that case the collateral circulation is mainly by way of the internal mammary and superficial epigastric veins. Dilated veins and cyanosis may be caused also by aneurism or chronic mediastinitis.

Rarely one of these mediastinal growths presses on the thoracic duct and causes a true *chylous ascites* which may be accompanied by chylous pleural effusion. *Pleural effusion* is frequent; often this is bloody, very rarely chylous. Rapid re-accumulation after tapping is characteristic.

In a number of cases a *tumor* is visible in the neck, either in the sternal notch or above the sternoclavicular articulation. Careful inspection of the neck may reveal deviation of the trachea from the midline, or the trachea is seen to ascent a trifle obliquely from the sternal notch, both indicative of an intrathoracic mass pressing the trachea to one side.

In a few cases the *position of the patient* is characteristic. Some assume an attitude with the head bent forward and the chin resting on the sternum. In one patient an ulcer of the forehead was produced from pressure on a table as the patient sat bent over. In other cases the greatest comfort is found with the head thrown back. Some can lie only on one side. The majority of patients find most ease propped up in bed in an almost sitting posture.

Cachexia may be found, but many patients maintain a surprisingly good state of nutrition. Moderate irregular *fever* occurs in a number. This is particularly true of the Hodgkin's disease group. It may be present before a tumor mass is demonstrable. Sometimes this fever may intermit for a varying time to recur. This cycle may be repeated a number of times.

Palpation yields additional data about thoracic deformities and pulsation. Palpation of the neck and axilla for tumor extensions or metastases is very important. Particularly is this true of the sternal notch. Here deep palpation may show a tumor mass in the upper mediastinum. Excision and microscopic study of accessible metastatic or extension nodules will yield a positive diagnosis. In all cases of suspected mediastinal mass the larynx should be palpated. In some cases it will be found fixed, no longer ascending and descending with deglutition and respiration. This is due to a mass pressing on the trachea and bronchi and fixing them. In other cases a tracheal tug, synchronous with the heart beat, will be found. This has been reported in mediastinal tumor, but is far more common in aneurism.

In a certain number of cases *percussion* reveals no evidence of any tumor mass within the chest. In an occasional case in which the tumor occupies the posterior mediastinum and produces no dulness anteriorly, percussion over the spines of the dorsal vertebræ may give an abnormal note, such as occurs in some cases of tuberculosis of the peribronchial lymph nodes, without there being any demonstrable dulness elsewhere in the back.

However, in the larger number there is a localized area of dulness in the region of the manubrium sterni which gradually increases in size with the growth of the tumor. Not infrequently such an area shows not a smooth, rounded outline, but an irregular contour, suggesting a lobulated mass. Most frequently the area of dulness is small, extending a short distance on either side of the manubrium, though it may be large, involving the greater part of the anterior thorax on one side. It may be apparent also in the back. The fact that the outline of dulness, although extensive, does not correspond to the anatomical position of a lobe or lobes of the lung and does not occupy dependent portions of the thorax, in most cases serves to distinguish it from one due to pulmonary consolidation or fluid in the pleural cavity.

Over the area of dulness, tactile and vocal fremitus is greatly decreased or absent. *Auscultation* of the dull area not infrequently is negative. In some cases, when there is dulness over the manubrium, there is an increased transmission of tracheal respiration; in others breath sounds are distant or even absent over the dull area. Auscultation outside of the area of dulness may reveal normal breath sounds, or one side of the chest may show suppressed breathing or almost total absence of respiratory sounds. On the other hand, auscultation frequently reveals numerous medium and coarse rales, often piping or sonorous, in one or both lungs, indicative of a more or less generalized bronchitis, resulting mainly from pressure. *Laryngoscopic examination* often shows paralysis of the vocal cords. The *pupils* may be unequal, as pressure on the sympathetic nerves may produce dilatation of the pupil during the irritative stage and constriction when the nerve bundles are destroyed. In a very few cases the tumor invades the spinal column and produces pressure on the spinal cord, with consequent paralyses.

Diagnosis.—The physical signs with the symptoms lead to the correct diagnosis in most cases. Roentgen-ray and fluoroscopic examination is the most important means of diagnosis. The nature of the neoplasm, whether malignant or benign, is shown chiefly by the course and by the extent and rapidity of development of pressure symptoms.

The *roentgen-ray or fluoroscopic examination* yields a very characteristic picture showing a definite abnormal shadow in the mediastinum. This may have a smooth rounded or scalloped contour sharply demarcated from adjacent lung fields or the border may be more ill-defined and irregular indicating invasion of the lung tissue. With the fluoroscope the definite expansile pulsation of an aneurism can be readily distinguished in the majority of cases from the slighter changes in contour of a neoplasm. Fluoroscopic examination in oblique and lateral positions is particularly important in the detection of smaller neoplasms and those in the posterior mediastinum either above or behind the heart.

In very few cases the *radial pulse* is smaller on one side, this being much more common in aneurism. Moreover, inequality of the radial pulses occurs in a number of other conditions, as in an anatomical anomaly of the radial artery of one side, in old hemiplegias, in arteriosclerosis more marked in one radial, in obstruction at the mouth of the artery by sclerotic processes in the aorta or innominate, and by any form of pressure obstruc-

tion in the course of the vessel. On the other hand, high-grade signs of venous obstruction point to neoplasm.

Diagnosis from *tumors of the lung* is difficult, because these tend to invade the mediastinum early, and many of the symptoms and physical signs usually given in a consideration of tumors of the lung are due to the mediastinal portion of the tumor. After the mediastinum becomes involved, it is often impossible to tell whether the tumor was primary in the lung or in the mediastinum. A history of onset with cough and blood-stained sputum without any evidence of pulmonary tuberculosis, particularly in a person over fifty years of age, strongly suggests a primary bronchiogenic tumor of the lung. Portions of the tumor may be expectorated and detected in the sputum. This is unlikely in mediastinal tumor. Localized dullness of a wooden quality in the pulmonary area suggests a tumor in the lung. Vocal and tactile fremitus is decreased over this region and breath sounds are usually weak, not bronchial, in character. In some cases of tumor of the lung a change from a tympanitic to a dull percussion note during several days' observation, with a probable return to the original condition later, occurs. This is due to a previous atelectatic portion of lung refilling with air as its bronchus becomes free. These signs in the absence of any evidence of considerable mediastinal growth (pressure symptoms) point to a primary tumor of the lungs rather than to a primary mediastinal tumor. Bronchoscopy makes possible the early diagnosis of lung tumors originating in bronchi or compressing bronchi. Radiographic examination often will differentiate a tumor of the lung from one of the mediastinum. If it shows areas of calcification the condition probably is tuberculosis.

Treatment.—Deep roentgen-ray treatment usually will greatly reduce the size of these neoplasms and completely cure all pressure symptoms. Relief sometimes takes place in an amazingly short time. Unfortunately, the change is never permanent and usually it persists only a few months; sooner or later the tumor increases again in size and the symptoms recur. Repeated treatments will repeat the symptomatic improvement for a limited number of times, but soon a stage will be reached when there is no further response to roentgen-ray treatment and death ensues. No permanent cure by radiation is probable. Not all tumors of this group react equally well to the roentgen-ray. It is thought by most observers, that, besides the marked amelioration of symptoms resulting from radiation with a consequent increase in comfort, there is a prolongation of life following roentgen-ray treatment. However, some untreated patients live quite long and it is difficult to get sufficiently large groups of thoroughly radiated and non-radiated cases as a satisfactory basis of comparison. So one is not justified in saying that radiation surely prolongs life. However, it is certain that it affords relief, even if temporary, of such degree to make this form of therapy indicated for all patients, not withstanding the uncomfortable reactions that follow the needed therapy. It is generally considered that the roentgen-ray is more effective in these cases than radium.

When pleural effusion develops, thoracentesis should be done as often as the effusion causes dyspnoea and other symptoms. If the effusion

recurs rapidly, it is advisable to drain the pleural cavity by introducing a small rubber catheter between the ribs by means of a trocar. This catheter should be connected by rubber tubing with fluid in a drainage bottle so arranged as to cause siphonage, all being kept sterile. In this way continuous drainage can be provided and the patient relieved. At times the tube should be pinched off temporarily with forceps since with too complete drainage the pain of a dry pleurisy may ensue.

By medicinal means pain and cough may be relieved and some control afforded for expectoration and dyspnœa, not helped by the above methods.

Modern surgery makes it possible to enter the mediastinum and make thorough exploration. Unfortunately the nature of these neoplasms prevents eradication complete enough to make a radical cure. So far relatively little attempt has been made to relieve pressure by removal of part of the sternum and ribs, a method analogous to a decompression operation for increased intracranial pressure. Palliation in suitable cases is probable from such a surgical operation.

Sarcoma.—An occasional case of spindle-cell sarcoma of the mediastinum has been reported and a still rarer one of chondrosarcoma. Symptoms and treatment are the same as for lymphosarcoma.

Endothelioma.—Only a few cases of endothelioma of the mediastinum have been reported. It is doubtful whether true endotheliomas arise from the mediastinal tissues. Those described probably have started from the pleural endothelium (mesothelium) and extended into the mediastinum. The symptoms produced in the mediastinum are those of other extensive secondary malignant growths there. With these are symptoms and physical signs due to development in the pleura.

Carcinoma.—Primary carcinoma is not frequent in the mediastinum as has been very generally, although incorrectly, supposed. Aside from carcinoma arising from the œsophagus, trachea, and bronchi, the only epithelial structures serving as possible sources for carcinomas are the thymus, misplaced or accessory thyroid, and fetal remains separated in the development of the respiratory or alimentary tract. The thymus normally disappears before the age of proneness to carcinoma comes; intrathoracic thyroid more usually produces intrathoracic goitre and is considered in that connection; fetal remains are excessively rare as a source. If we eliminate cases which should be classed as sarcomas, lymphosarcomas, secondary carcinomas, pleural endotheliomas, and bronchial carcinomas, few cases remain. Josephson, working under Baumgarten, collected 46 cases of so-called mediastinal carcinoma. Only 11 of these were studied and described sufficiently well to apparently deserve the diagnosis according to Josephson and Hoffman, who think that several of these 11 are wrongly included. Löhrisch collected the cases of mediastinal tumor reported in 1896–1901 and finds but 2 of carcinoma and 2 with adenomatous parts. In 1906 Zypkin reported a case. Since 1906, 2 cases, those of Perkins and Roubier, seem to justify the diagnosis of primary carcinoma of the mediastinum. Another, that of Steenhuis, possibly belongs in this group, though as it encroached on the œsophagus and is described as metastasizing into its mucous membrane, it may, perhaps, be grouped more correctly as a tumor primary

in the œsophagus. Two cases of dermoid cyst underwent carcinomatous change, and might also be grouped here.

A description of symptomatology based on such a small group of cases must be imperfect and is scarcely warranted. These cases, however, do show the tendency to occur in older people as would be anticipated. An invasive growth and the frequency of venous obstruction with localized œdema, cyanosis, and venous dilatation are to be regarded as points favoring the diagnosis of carcinoma rather than sarcoma and lymphosarcoma. However, before any very definite differential points can be given many more cases must be carefully studied during life and the diagnosis made certain by careful histological study after death. Roentgen-ray treatment of mediastinal tumors, other than the lymphosarcoma group, is likely to produce little improvement but it should be tried in every case.

Simple Cyst.—Although much more infrequent than dermoid cysts, simple cysts may occur in the mediastinum. Usually these have been small and lined by ciliated epithelium. Among the accounts of 12 cysts reported, it was found that 6 were situated in close proximity to the bifurcation of the trachea, 4 near the lower end of the œsophagus, and 1 in the anterior mediastinum 4 cm. above the tracheal bifurcation. Almost all were small and in most of the cases the cyst produced no symptoms. In Fletcher's case, a girl, aged six years, there was cough for one week, with dyspnœa and cyanosis for three days before death.

Bramwell's case is of interest because of the difficulties in diagnosis. It occurred in a man, aged fifty years, with a history of syphilis and hard drinking for several years. He entered the hospital on account of nephritis. It was then found that he had visible, palpable pulsation over the second right interspace near the sternum, localized dulness, and a slight systolic thrill. In this region a systolic murmur could be heard and the aortic second sound was accentuated. There was neither pain nor pressure symptoms but the diagnosis of aneurism seemed justified. A year later he died from nephritis and autopsy showed a cyst in the mediastinum. The pulsation was transmitted and the accentuated second sound was associated with the nephritis. The systolic murmur came from a thickening of the aortic valve.

Dermoid Cyst and Teratoma. Among the more uncommon tumors are those which may be grouped together as dermoid cyst and teratoma. This group consists of tumors varying in complexity from a simple cyst lined by epidermis with its appendages (hair follicles, sebaceous glands, or sweat ducts) to solid tumors made up of a variety of tissues in complex arrangement. Between these two extremes all gradations of complexity are met and it is difficult so to define the terms, dermoid cyst and teratoma, that two distinct groups can be made. Furthermore, all have much in common as to origin, course of development, and symptomatology, and they are best described together. As might be expected, almost all of these tumors are benign in the sense that they do not metastasize. However, a very few, especially the teratomas, have formed metastases more often of a sarcomatous nature. In 1912, Ceelen described a dermoid cyst in whose wall carcinomatous degeneration had taken place and metas-

tasis had ensued. This he claimed to be the first case described of this type but in the next year Schusterówna in literature not available to the writer appears to have described a similar case of cancer in the wall of a dermoid cyst of the anterior mediastinum.

Dermoid cysts and teratomata do not occur very frequently. Hare in 1889 among 288 cases of mediastinal tumor reported only 10 dermoid cysts. At the end of 1901 the writer was able to collect 40 cases of dermoid cyst or teratoma and Morris in 1905 brought this number up to 57. In 1907 the writer reported 2 cases of solid teratoma of the mediastinum and found one other new case of this type in the literature. To these are to be added 31 additional cases from the literature which increase the total to 88 cases of dermoid cyst and teratoma from the first reported by Gordon in 1823 to July 1, 1924. Of these, 12 seem to belong to the teratoma group in contrast to dermoid cyst.

From the clinical standpoint it is important to keep in mind a few of the structural peculiarities of these tumors. The content of the cyst is a greasy, gray to yellow, semisolid material in which hair is often mingled. If this material escapes to the surface of the thorax through a fistulous communication or is coughed up as a result of rupture into a bronchus, it may be recognized and a correct diagnosis made as happened in a number of cases. The patient's statement of coughing up hairs or finding them on the tongue is frequently too much for the credulity of the physician. The tumor often includes bone, cartilage, or teeth, all of which will give a characteristic shadow on roentgen-ray examination, and lead to a diagnosis. As a rule they grow slowly.

The primary position of the tumor is usually in the upper half of the thorax, wholly or in part immediately behind the manubrium sterni. A smaller number are situated in the lower half of the thorax between the heart and the adjacent lung. In several cases the tumor extended into the neck. Development of a tumor in the upper part of the anterior mediastinum beyond a certain point would be resisted in front by the bony wall of the thorax, and behind by the great vessels and trachea supported by the vertebral column. Growth would be possible in three directions, upward through the superior aperture of the thorax, laterally into the pleural cavity, and downward between the heart and lungs, and these three directions of expansion occur in reported cases. For some tumors not situated in the upper anterior mediastinum migration from a previous position can be assumed to have taken place as the tumor increased in size.

In almost every case adhesions to some adjacent organ are found. The tumor is most frequently bound to some part of the lung and almost as often to the pericardium. Less frequently they are attached to other structures, as chest wall, diaphragm or great vessels. These tumors, though occupying a position surrounded by vital organs and generally in actual union with them, do not as a rule produce great destruction of adjacent structures. In 1 case the aorta was eroded, in a second there was a communication between the tumor and the pericardial cavity; in a number of cases they eroded into the lung and formed a communication with the bronchus.

These tumors are far more frequent in young adults. Of the reported cases nearly 62 per cent. came to operation between the ages of eighteen and thirty years. Sex has no apparent influence on their occurrence.

Symptoms.—The *onset* is nearly always gradual. There is usually a latent period during which the tumor gives no evidence of its existence. Ordinarily this continues up to the time of puberty when the tumor begins to grow more or less rapidly, and as it increases in size, begins to press on adjacent structures and symptoms appear. This constitutes the period of activity. While this is true of most cases, in others symptoms have appeared at an earlier or later period or the tumor remained latent throughout life, to be an accidental finding at autopsy.

The onset of an active stage is by no means characteristic; indeed, it is seldom that the condition has been correctly diagnosed early. The common early symptom is dyspnoea after exertion, frequently associated with pain in the chest, at times with cough or a feeling of pressure. Less commonly pain and hemoptysis have been the initial symptoms. With progress of the growth of the tumor, dyspnoea almost always becomes prominent. In the earlier stages it is apt to be intermittent, greatly aggravated by exertion, and generally accompanied by cough with expectoration, frequently blood-tinged. In the later stages difficult breathing is more constant and severe, and may become so extreme as to cause death. Dysphagia does not occur.

Pain is frequent, although it may be slight or not present at all. It is usually sharp, seldom dull and aching. There is nothing typical in the *cough*. The sputum, however, is of very great importance and should be carefully examined in every suspected case. The quantity varies greatly; at first it is small in amount but later may become very copious. The sputum may be (1) that which comes merely from the bronchi or (2) that which comes from bronchi and cyst cavity by way of a perforation into a bronchus. The first is in no way characteristic; it results from the bronchitis following pressure on the trachea or bronchi; it is the sputum of a chronic bronchitis or of a bronchiectasis and may occur with any mediastinal mass. The second may be characteristic and in some cases is pathognomonic. Search should be made for epithelial cells, resembling those from the horny layer of the skin, for fat droplets, fatty acid and cholesterin crystals, and for hairs. The finding of the last is absolutely diagnostic, the others highly suggestive of dermoid cyst. It is not likely that the sputum will aid in the diagnosis of a solid teratoma. In 21 of the reported cases there was a communication between the cyst and a bronchus; in 11 of these, hair was expectorated and 8 were correctly diagnosed.

Hemoptysis is quite common but is usually late. It may be severe enough to cause death. In other cases there is continued but slight loss of blood, so that the sputum is almost always blood-tinged.

The *course* is relatively a slow one, a period rather of years than of months. This is in strong contrast to cases of malignant disease of the same region.

Physical Signs.—The patients are usually well nourished and show no evidence of cachexia. The superficial veins of the thorax are not distended; there is no local oedema. The radial pulse is equal on the two sides. In no

case has paralysis of the vocal cords been noted. Frequently the tumor produces a fulness or bulging of the chest wall, usually anteriorly. This is oftenest in the upper part of the chest from the level of the second to the sixth ribs, but may be elsewhere. This asymmetry of the chest persists for months or years, showing little or no change. The tumor may appear in the neck through the superior aperture of the thorax, and in some of these fluctuation can be made out. In others pulsation may be present but is not expansile in character. Fistulous communication between the cyst and skin surface may form with discharge of characteristic cyst contents.

If the tumor is of moderate size, *percussion* almost always reveals an irregular area of flatness or dullness over which breath sounds and vocal and tactile fremitus are diminished. This is practically always the case when the tumor deforms the chest and corresponds to the prominence. The dullness is usually in front but in some cases is situated behind. Again, there may be dullness anteriorly and posteriorly with intervening resonance or almost the entire right or left half of the thorax may be dull. On *auscultation* very frequently moist or dry rales are heard throughout the lung on the side of the tumor, not infrequently on both sides. Over the dull area produced by the tumor breath sounds are absent or decreased in intensity. When the tumor is large or situated low down, displacement of the heart occurs or the liver may be pushed downward.

Diagnosis.—When hairs are expectorated, or escape from a fistulous communication with the skin, the diagnosis offers no difficulty. Fat droplets, fatty acid, and cholesterolin crystals or squamous epithelium, similarly escaping from the cyst, give a good clue to the diagnosis. Exploratory puncture has yielded a correct diagnosis in some cases, having been done in several cases under the impression that pleurisy with effusion existed. The roentgen-ray examination, besides showing the situation of a tumor mass and its smooth rounded contour characteristic of a cyst, may reveal its dermoid and teratomatous nature, when bone or teeth form a part of the growth.

A probable diagnosis can be made when we have evidence in a young adult of a mediastinal tumor of slow progress. The duration of malignant disease is rarely as long as one year. Cachexia, common in malignant disease, is rare in dermoid cysts and teratomas. Pressure signs, such as œdema, cyanosis, distention of superficial veins, inequality of the pupils, and laryngeal changes, are not found with mediastinal tumors of this group, except in those more infrequent ones which show malignant parts. The course of the latter is like carcinoma and sarcoma, and, like them dermoid cysts and teratomas are proved malignant when there is evidence of metastasis.

The diagnosis from aneurism is usually not difficult. A case similar to Buchner's, in which there was a communication between cyst and aorta, presents diagnostic difficulties, but such a condition is little to be expected and, if it occurred, the treatment would be that of aneurism, for such it was practically. Echinococcus cysts can be differentiated from dermoids only by an examination of their contents. Other benign tumors are rare and inflammatory processes present almost no difficulty.

Prognosis.—This, as compared with that of malignant tumors, is good, since the latter are almost invariably fatal in less than one year, but it is to be remembered that in dermoid cyst or teratoma, unless operated on, the chances for life for more than a few years are not very good.

Treatment.—Surgery presents the only hope of cure. Medical treatment, other than palliative, is futile and every patient should be given the chance of surgical treatment. Radical operation is rendered difficult by the proximity of vital organs, the frequency of extensive adhesions, and the danger of entering the pleural cavity with the production of a sudden pneumothorax. Simple drainage usually proves ineffectual and marsupialization can be done only rarely owing to the cyst being multilocular or to the presence of diverticula in a simple cyst or because the cyst has become infected. Improvements in surgical technique are increasing rapidly the possibilities of successful intrathoracic surgery and mediastinal tumors of this type may be regarded as reasonably good surgical risks. Of 20 cases operated on up to 1906, including those of early date, 70 per cent. were much benefited and a considerable number cured. According to Garré, up to 1922, 22 had been operated on with the survival of 16. Since 1912 of 10 cases found reported in the literature as operated on cure was effected in 7 by removal of the tumor, while 3 died following operation. These results in a condition otherwise hopeless certainly justify an attempt at surgical removal in all cases especially if done when the patient's general condition is reasonably good. The actual results depend in very large part on the situation of the tumor in relation to vital structures and especially on the kind and extent of adhesions to them.

MEDIASTINITIS

Inflammation is not infrequent in the mediastinum, but mediastinitis is not often recognized. This is due to the fact that most often the mediastinal inflammation arises as a complication of some process elsewhere, whose symptoms mask those of the mediastinitis itself.

Inflammation in the mediastinum may be acute or chronic. In the acute there may be simply exudation, serous, fibrinous, or purulent, into the loose areolar tissue, or tissue disintegration may take place with abscess formation. No sharp line can be drawn between the two types, acute mediastinitis and mediastinal abscess; whether the one or the other occurs, depends on the cause, duration, and severity of the process. For this reason in considering acute inflammation it does not seem advisable to consider separately simple mediastinitis and mediastinal abscess, but they are discussed together as stages of mediastinal inflammation, the former mild, the latter severe, their symptoms varying chiefly in degree. In chronic mediastinitis there may be connective tissue proliferation with mediastinal adhesions or chronic abscess, the latter almost always tuberculous in origin.

Acute Mediastinitis.—This, whether in the form of infiltrating exudation or abscess, occurs in the loose areolar and fatty tissue which surrounds the mediastinal organs. The seriousness of inflammation in this region depends on the facts that the mediastinum is a closed space structurally

difficult of drainage either by nature or operative means, and that extension into vital structures is apt to take place.

Acute inflammatory processes in the mediastinum may be divided on an etiological basis into three groups, traumatic, extension, and metastatic. Of these the *traumatic* is the most important, not on account of its frequency, but because trauma so often leads to abscess formation, rendering this group of cases most serious. Inflammation by *extension* is more common, but in many cases, apart from the severity of the primary disease, is of no very great importance, at least in the acute stages. *Metastatic* inflammation in the mediastinum is the rarest of the three.

Blows on the chest, particularly over the sternum, with or without fracture of bones, frequently cause diffuse suppurative mediastinitis or mediastinal abscess. Goodhart reported an instance in which, following a blow on the chest from a log of wood, pain in the chest and great dyspnoea developed, with a fatal result in six days. Autopsy showed purulent infiltration of the mediastinum, with double pleuritis and pericarditis. A somewhat similar case followed a blow on the chest by a red-hot bar of metal but this patient recovered. Crushing injuries to the chest or spinal column, if not immediately fatal, sometimes produce this condition, as in an instance at the Boston City Hospital, in which, with suppuration of the tissues of the forearm about a Colles' fracture and a fracture of the twelfth dorsal vertebra, there was an abscess of the mediastinum. The tissues of the anterior mediastinum were matted together, quite firmly attached to the sternum, and infiltrated with pus, which was most abundant at the level of the third costal cartilages. The purulent fluid extended down between the pericardium and the right pleura.

Sometimes trauma appears to be the cause when there is little evidence of direct injury to the thorax. Such an example is given by Laird in a man who fell out of an apple tree several days before coming to the hospital. This fall gave him a thorough jarring but did not cause any evident local injury. Severe pain in the neck, head, and chest developed later and the region about the sternoclavicular joint became swollen, reddened, and cedematous. Incision over this evacuated about a pint of pus from the anterior mediastinum. Complete recovery followed.

Penetrating wounds of the mediastinum, with or without injury to the trachea or œsophagus, form another group in which mediastinal inflammation results. Günther reports a mediastinal abscess following a dagger wound penetrating the sternum. Traumatic injury or perforation of the œsophagus, trachea, or bronchi by a foreign body is apt to produce mediastinal inflammation. Similar results may follow instrumental perforation during operative procedures, as in passing sounds in the œsophagus, as in a case reported by Hacker. In this case the communication between the œsophagus and mediastinum was demonstrated by an ingenious test. Gauze impregnated with a 2 per cent. solution of potassium ferrocyanide was inserted in the cavity through the drainage wound, and the patient then swallowed a small amount of 2 per cent. solution of citrate of iron. The gauze was then removed and found to be blue where the two solutions came in contact, thus demonstrating the opening

in the œsophagus and also indicating its location. The course of healing was followed by the same means until it was evident that the œsophageal opening had closed. This happened fourteen days after the operation.

In the group of *inflammations by extension* come the very numerous cases in pneumonia in which the mediastinal tissues are infiltrated with serum or seropus. This is frequently seen at autopsy, but the mediastinitis usually gives little or no indication during life of its presence and it is rare for it to go on to abscess formation. In the influenza epidemic the pneumonic process, largely bronchopneumonic in type, was often complicated by mediastinitis and not infrequently there was an emphysema of the mediastinum in addition. Extension into the mediastinum of an acute pleuritis, secondary to pneumonia, is common, and any inflammatory condition of the lung, as abscess, gangrene, tuberculous cavity, etc., can so act. Cases of pneumonia with pericarditis or peritonitis frequently show mediastinitis, probably extending from the complicating lesions rather than from the primary pneumonia.

The tendency of an acute pericarditis to extend to the mediastinal tissues is well recognized and is not an uncommon postmortem finding. In some cases of general peritonitis without pericarditis or pleuritis there is an associated inflammatory infiltration of the mediastinum, probably the result of a lymphatic extension through the diaphragm.

Any ulcerative process in the trachea, bronchi or œsophagus tends to produce mediastinitis by extension or by perforation. This is particularly true of perforation of the œsophagus owing to food particles escaping and infecting the surrounding tissues, frequently causing abscess.

Inflammation of the mediastinal lymph nodes, if the nodes soften and break down, may lead to extensive inflammation of the mediastinum. This more commonly follows tuberculosis of the lymph nodes and the abscess is apt to be chronic in nature.

Acute osteomyelitis of the sternum, ribs, or vertebræ may be the starting point for mediastinal inflammation.

Inflammation may extend into the mediastinum from the neck. This is rare from the superficial tissues, since the downward path of the process is well guarded by fasciæ. From the tissues about the larynx and trachea, on the other hand, extension is easier, while along the prevertebral region it is almost the rule in extensive processes, except from those in the immediate subcranial region and about the upper cervical vertebræ, where lateral extension is commoner. Inflammatory conditions of the pharynx, larynx, trachea, œsophagus, and lower cervical vertebræ are apt to extend to the deep cervical tissues and from them may descend into the mediastinum.

Metastatic inflammation of the mediastinum may occur as a complication or sequel of a variety of infectious and pyemic conditions. Cases have been reported during or following erysipelas, variola, typhoid fever, septic endocarditis, and rheumatic fever. Examples are cited by Hare and by Hoffmann.

Notwithstanding this variety of possible causes a number of cases of mediastinal inflammation have been reported the etiology of which is

by no means clear. As in other regions of the body, we regard them as probably infections whose portal of entry is not discovered.

Chronic Mediastinitis.—Following the diffuse infiltration of an acute mediastinitis, granulation tissue may form, resulting finally in scar tissue, binding together the mediastinal structures and interfering with their function. This is especially likely to take place with pericarditis and produce a mediastinopericarditis. Rarely, if ever, are the digestive or respiratory tracts interfered with by such a chronic process. Occasionally the veins are obstructed and very infrequently the thoracic duct. A case illustrating the latter is given by Comey and McKibben in which from chronic tuberculosis involving the apex of the left lung the process extended to the mediastinal tissues and involved the thoracic duct in scar tissue with consequent obstruction, causing chylous ascites. A recent case of tuberculous origin at the Peter Bent Brigham Hospital showed marked cyanosis of the face, neck, arms and upper thorax.

Chronic abscess, practically always tuberculous, is an extension process from broken down bronchial lymph nodes or carious bone. Usually abscess of the anterior mediastinum arises from the former. Tuberculosis of the sternum and anterior ends of the ribs leads to disease of the anterior mediastinum, while from dorsal Pott's disease comes abscess of the posterior mediastinum. Chronic abscess pathologically differs in most respects but little from acute abscess; clinically, except for longer duration and less marked febrile disturbance, they are similar and the symptoms of the two will be considered together. Abscesses of tuberculous origin later may be accompanied by general miliary tuberculosis which is rapidly fatal.

Abscess of the mediastinum, whether acute or chronic, after remaining localized for a time, is apt to rupture into some of the mediastinal organs or on the skin surface. Perforation into the œsophagus may occur and the pus be vomited, or into the trachea or bronchi and the pus be coughed up or inspired into the lung. Extension to the pleural cavities causing empyema is common and penetration of the pericardium may take place with resultant pericarditis. Rupture into the aorta or large mediastinal veins has been reported. In a number of cases the pus reaches the body surface along the upper border of the sternum or it may burrow for some distance in the deeper tissues and reach the surface at various points on the thorax. In a woman, aged thirty-five years, after many weeks of pain, a lump formed over the upper part and left side of the sternum from which pus was evacuated. A sinus persisted for two months, accompanied by severe pain and fever. The skin over the front of the sternum and for 8 inches beyond its left border became red, œdematous, and apparently undermined. A sinus extended to the second left sternocostal articulation, where there was bare bone. Finally, the sternum was trephined, freely opened, and drained. Recovery was rapid and complete. Sometimes the mediastinal suppuration extends to the neck and the abscess may rupture in the region of the sternal notch or the sternoclavicular articulation.

Obviously in conditions with so various an etiology as mediastinal inflammations, sex or age are of no special import. As might be expected,

where trauma plays an important role in etiology, males more often are affected, and the young rather than the old, but no very striking age preponderance is found.

Symptoms and Physical Signs of Acute and Chronic Mediastinitis.—These vary with the extent and character of the process. Many times inflammation exists in the mediastinal tissues associated with inflammatory conditions elsewhere, without there being any symptoms pointing to the mediastinal process. In acute inflammatory conditions, thoracic *pain* is the most common symptom, and this is usually of a throbbing character. With this, fever, a rapid pulse, and the facies of a septic process are associated. With simple infiltration, pressure symptoms are not common, but with abscess formation, whether acute or chronic, they develop and there is a varying combination of dyspnoea, dysphagia, venous obstruction, and pressure on nerve trunks, with the train of symptoms discussed under tumors. Pain due to nerve-root pressure may lead to errors in localizing the process, as where pain in the intercostal roots is referred to their terminals or with involvement of brachial roots is localized in the arm.

In lesser degrees of involvement, physical signs are lacking unless, as frequently happens, there is extension to the skin surface, with localized redness and induration, with or without ulceration and sinus formation. Such extension usually takes place in the upper intercostal spaces near the sternal margin. It may appear over the sternum, especially at the junction of the head and body. In the suprasternal notch or above the sternoclavicular joint is another site. More rarely penetration takes place behind, in the region of the spinal column. Dulness may be elicited on percussion. With larger collections of pus, Hacker called attention to a shifting or disappearance of this dulness with changes in the patient's position. More probably this sign will be given by cases in which, with perforation of the œsophagus or respiratory tract, there is a mixture of air and pus within the mediastinum. If emphysema is present, auscultation reveals a clicking, crackling sound, synchronous with respiration or heart beat. With much air, resonance replaces the usual dulness on light percussion over the sternum. Without emphysema one may hear a scratching or leathery friction rub with respiration or heart beat. There may be bulging of the chest wall, fluctuation or even pulsation synchronous with the heart beat. In a few cases mediastinal tumor or aneurism is closely simulated.

The course of mediastinal inflammation is usually rapid. Generally it is an acute condition developing in a few days, and extending over a short period only. More rarely it develops slowly over a period of weeks. The latter cases are often tuberculous in origin.

Diagnosis.—This depends largely on the combination of symptoms of mediastinal pressure with the general features of a septic process. Abscess of tuberculous origin presents most difficulty. When there is extension of the process to the skin surface the diagnosis is usually easy. In connection with these cases it is well to bear in mind that in some cases of mediastinal tumor there is fever unaccounted for by any secondary inflammatory condition, although the latter may be present, as in a Boston City Hospital case of extensive lymphosarcoma of the anterior mediastinum. In

this case perforation of the left primary bronchus had taken place. The tumor showed hemorrhage, and on microscopic examination there was much fibrinous and leukocytic infiltration, so that many sections appeared to be from an inflammatory rather than a neoplastic process.

Treatment.—This is purely surgical. In the earlier stages poultices may aid; evacuation is called for when pus forms. For pus in the anterior mediastinum operation is relatively simple; in the posterior mediastinum access is much more difficult.

ECHINOCOCCUS CYSTS OF THE MEDIASTINUM

Echinococcus cysts occur in the mediastinum, but are very rare. Hare tabulated 8 cases and Hoffmann 4 cases. If the cysts are large enough to produce pressure, the symptom would simulate those of a tumor of slow growth.

ABDOMINAL MEDIASTINAL CONTENTS

Hernia.—A rare condition is extensive hernia of abdominal viscera through the diaphragm into the thoracic space. Congenital defects of the diaphragm in the stillborn or in those dying soon after birth are the commonest causes. In such cases the abdominal viscera more commonly occupy the pleural than the mediastinal space. Hernia of congenital origin also occurs in the adult but is more usually associated with some injury or strain of the diaphragm. Just behind the xiphoid cartilage the diaphragm is structurally weak. Here and behind, where there are openings in the diaphragm for the passage of vessels and the œsophagus, hernia is prone to occur, with the entrance of abdominal viscera into the anterior or posterior mediastinum, respectively. The stomach and colon are the organs more commonly concerned. These cases may be symptomless; nausea and vomiting may be associated with displacement of the viscera or there may be symptoms of pressure on the mediastinal structures. Abnormal areas of tympany on percussion arouse suspicion of such a hernia. The presence of gurgling sounds in the mediastinum is the physical sign of most aid in diagnosing this condition. Roentgen-ray study after a barium meal easily makes a positive diagnosis when physical signs suggest the condition. Death from intestinal obstruction is not uncommon in these cases. Surgical interference offers the only chance of relief, but is too dangerous to be advised except in patients with obstruction or other very serious disability.

Modern roentgen-ray methods of studying the gastro-intestinal tract after a barium meal show that the upper part of the stomach not infrequently herniates above the diaphragm in the region where normally the œsophagus comes through. In a comparatively short time several such cases have been seen at the Peter Bent Brigham Hospital. Symptoms are merely those of vague or indefinite character suggesting some sort of gastric disturbance. Diagnosis without roentgen-ray study would seem impossible. No special treatment is indicated in these, as symptoms do not warrant surgical operation, at present extremely difficult and highly dangerous.

Hemorrhage. Slight mediastinal hemorrhages may occur in purpura, the hemorrhagic exanthemata and other severe infectious processes.

Severe hemorrhages are of traumatic origin or due to the rupture of aneurisms. If the person survives the immediate injury, the blood is gradually absorbed without any harm. In some cases of considerable hemorrhage there are pressure symptoms.

Emphysema.—This is a rare mediastinal lesion. Air may enter the mediastinal tissues as the result of trauma of the thorax, tracheotomy, ulceration of the œsophagus, trachea, or bronchi, pertussis or pulmonary disease. Usually there is a history pointing to some one of these causes. Examination shows partial or complete absence of cardiac dulness and in its place a tympanitic percussion note. Cardiac pulsation is neither visible nor palpable and the heart sounds are muffled. Synchronous with the heart beat there are fine crackling sounds, usually systolic in time, sometimes both systolic and diastolic. Usually there is also an accompanying emphysema of the neck, more often on the left side, and possibly of parts of the thorax. In most cases there is respiratory distress and often dysphagia.

Mediastinal emphysema is to be diagnosed from pneumothorax and pneumopericardium. In pneumothorax the heart is displaced and the cardiac impulse can usually be made out in an abnormal position. In both pneumothorax and pneumopericardium the fine crackling sounds synchronous with the heart beat are absent and there is no accompanying subcutaneous emphysema. With mediastinal emphysema the metallic tinkling sound is not present and there is no change in the position of the area of tympany with change of position. Mediastinal emphysema in itself is not serious and the air is readily absorbed. In many instances it accompanies a serious condition and may be a terminal event. The emphysema requires no treatment.

DISEASES OF MEDIASTINAL LYMPH NODES

Tumors have been considered and abscesses of lymph-node origin were discussed under mediastinitis. There remain simple hyperplasia, pigmentation, sclerosis, and tuberculosis. These will be considered in certain particulars of local import aside from general diseases of the lymph nodes and tuberculosis described elsewhere.

Simple Hyperplasia.—In a variety of conditions the mediastinal lymph nodes become moderately enlarged, due to the action of bacteria or toxic substances, and associated with lesions of the territory drained into the mediastinal lymph nodes or with general conditions affecting the lymph nodes of the body. The peribronchial group is more often affected in this way, although both the anterior and posterior mediastinal group may be. As a rule these changes produce no symptoms. Occasionally in children, with repeated or prolonged attacks of bronchitis, there is considerable enlargement of the peribronchial lymph nodes, enough to produce pressure on the bronchi and irritation of the bronchial mucous membrane. This causes cough which is often stubborn, tends to be paroxysmal and is apt to occur for the most part at night. The cough may resemble the whoop of pertussis but differs in its persistence and the absence of infection. It is rare to have any physical signs; if present they are similar to those described for tuberculosis of the mediastinal lymph

nodes. Treatment, aside from measures for the primary condition, should be along the lines of general hygiene.

Pigmentation and Sclerosis.—Carbon deposits are usually present in the peribronchial lymph nodes, and this is very marked in those whose daily occupation exposes them to an atmosphere laden with coal dust. The same conditions prevail for other occupations with similar exposure, as stone cutting and cutlery grinding. Other forms of pathological pigmentation are of very minor importance. In the great majority of persons this pigmentation produces no injury. If the condition is marked the lymph nodes are slightly enlarged and somewhat sclerosed, but this ordinarily produces no symptoms. Possibly a few cases of persistent cough may be due to the irritation of the bronchial mucous membrane by slightly enlarged lymph nodes. In some a more extensive chronic inflammation is set up with induration of the surrounding tissues and adhesions, which may lead to pressure on or perforation into mediastinal structures. Very often traction diverticula, especially those of the œsophagus, seem to be due primarily to the adhesion of sclerosed pigmented glands.

Softening and breaking down of the pigmented nodes may occur with perforation of adjacent viscera or abscess formation. A number of such cases have been reported. In most of them the bronchus, alone or with other viscus, has been perforated and putrid bronchitis and pulmonary gangrene produced. However, it is not always clear that these changes are due to the pigmentation and sclerosis alone, and it is probable that in some at least syphilis and tuberculosis have been factors. The symptoms are almost entirely the result of the adhesions with or without perforation and need no special discussion.

Tuberculosis.—Tuberculous lesions in the mediastinal lymph nodes are very common. In most cases they are associated with pulmonary tuberculosis or tuberculous caries of the vertebrae, ribs, or sternum. In a smaller number of cases the tuberculosis appears to be primary in the mediastinal lymph nodes; at least, that is the most prominent and most advanced lesion. This last form occurs especially in children.

In the mediastinal lymph nodes various tuberculous lesions occur. Of these there are three general groups, miliary tuberculosis, caseation and calcification with moderate enlargement, and proliferative lesions with tumor formation. The clinical importance of the second group is an indirect one: they form a source for tuberculous infection of other organs; by extension they produce mediastinal abscesses; they rupture into adjacent structures, bronchi, trachea, œsophagus, veins, arteries, or pericardium, with serious consequences. Apart from these the local process is practically symptomless. Occasionally the rupture of a caseous bronchial lymph node into an adjacent structure may be the cause of sudden death. The caseous mass, escaping into the respiratory tract, may obstruct the glottis and cause death by suffocation. Several such cases have been reported. Fistulous communication with the cutaneous surface may be formed, or with this may be combined perforation of a bronchus or the œsophagus, so that air or food may be expelled from the skin sinus.

The proliferative tuberculous lesions of the mediastinal lymph nodes

are not so frequent as the other two forms, but as a group they are of rather more clinical importance, since with them the lymph nodes form definite tumor masses which may not caseate. This form occurs in adults, but is much more common in children, in whom it forms an important group of tuberculous cases. Here we have large masses in the mediastinum, composed of enlarged lymph nodes, producing many of the pressure symptoms already described for tumors.

Symptoms and Physical Signs.—In many cases of tuberculosis of the mediastinal lymph nodes no symptoms result. In children dying of some of the acute infectious diseases, tuberculous lymph nodes are quite frequently found without there having been any symptoms during life pointing to them. When the lymph nodes are sufficiently enlarged and so situated as to produce pressure, a variety of symptoms results. A very important one is *cough* due to bronchial irritation which is apt to be persistent in the form of paroxysms of spasmodic cough, often resembling pertussis. Substernal pain may occur, but more characteristic is pain in the region of the fourth dorsal vertebra. Dyspnea may be present, as also dysphagia. Venous dilatation, oedema, cyanosis, hoarseness, and aphonia occur.

Physical examination is often negative. In some cases enlarged lymph nodes can be palpated in the suprasternal notch or fixation of the trachea during respiration may be detected. In a few cases dullness is elicited, especially behind in the region of the second to sixth dorsal vertebrae on one or both sides, near the midline or in front over the sternum. In other cases, with or without dullness near the midline behind, percussion over the spinous processes may give resonance different from that elicited under normal conditions. Koranyi pointed out that normally over the seventh cervical spine there is flatness; from the first to fifth dorsal spines there is a gradually increasing resonance, and, from the sixth to the eleventh, resonance. In cases with enlarged bronchial lymph nodes flatness continues below the seventh cervical and modified resonance extends to a lower level than in the normal. On auscultation increased transmission of respiration and voice, with a high-pitched bronchial or tracheal quality may be detected in these regions. This is the d'Espine sign, about which there has been discussion as to whether it points to enlarged peribronchial lymph nodes or a localized pneumothorax at the lung hilum. Smith called attention to a venous hum, heard over the sternum with the head thrown back, as a sign of enlarged bronchial lymph nodes. Wiederhofer attaches importance to a relatively loud expiration heard behind over the left bronchus. The roentgen-ray examination in most cases reveals the presence of enlarged or calcified bronchial lymph nodes. The other signs may be lacking when the roentgen-ray shows enlarged nodes and so it is of most importance in diagnosis.

Diagnosis.—Diagnosis in children in whom tumors are not so very common can be correctly made in many cases. In adults the difficulties are much greater, since, frequently, all the signs of tumor are closely simulated. Even confusion with aneurism may arise. The roentgen-ray usually yields a correct diagnosis.

Treatment.—This does not differ from that applicable to other forms of tuberculosis unsuited for surgery.

CHAPTER XI

DISEASES OF THE DIAPHRAGM

BY H. R. M. LANDIS, M.D.

UNTIL within the past few years the diaphragm has been ignored almost completely. Aside from diaphragmatic pleurisy and subphrenic abscess, textbooks dealing with diseases of the chest make no allusion to this remarkable structure, which, in many respects, is the most important factor in the respiratory act. Not only has the clinician neglected its functions, but the pathologist has made little effort to determine whether structural changes had occurred. That most astute of physical diagnosticians, Walter H. Walshe, long ago pointed out the rarity with which the diaphragm was examined postmortem and the consequent ignorance which prevailed as to the part it played in diseases of the thoracic organs and those of the upper abdomen.

Physiological Considerations.—The motor innervation of the diaphragm is still under discussion. It has been assumed that the lowest intercostal nerves send motor branches to the muscles in addition to the phrenic nerves. Schlaepfer¹ from experimental observation demonstrated that the phrenic is the only motor nerve of the diaphragm. He further states that the few clinical observations and necropsy findings on man point to the same arrangement in human beings.

The diaphragm is the chief means of inspiration. In its action it closely resembles the heart in its rhythmic repetition. It differs from the heart muscle, however, in that it is both a voluntary and an involuntary muscle. In common with the heart, it performs its work without conscious effort on the part of the individual, but unlike the heart, its action may be voluntarily arrested, increased or checked. The muscular action of the diaphragm differs from other muscles in that the duration of its action is from four to eight times that of the latter. It is therefore to be regarded as a tetanic movement of short duration (Landois).

During a normal inspiratory act, the two leaflets of the diaphragm contract. This causes the two dome-like projections to become flattened, and as a result the thoracic cavity is enlarged downward and the epigastrium and hypochondria bulge outward. In addition, the distal, arched muscular parts become flatter and are drawn away from the chest wall, to which they are closely applied during relaxation or the expiratory phase. The middle part of the diaphragm, upon which the heart rests, plays a very small part during quiet respiration but during forced breathing it is depressed, also, to a certain extent.

One of the chief functions of the diaphragm is to keep the lower parts of the lungs fully expanded. If this fails, and especially if the lung is forced upward by the unopposed abdominal muscles, the lower part of the

¹ *Bull. Johns Hopkins Hospital*, 1923, **34**, 195.

lung will collapse, just as failure of any portion of the chest wall to expand will lead to collapse of the underlying lung. In addition to the diaphragm, which is the chief means of inspiration under ordinary conditions, the sterno-cleido-mastoids, scaleni, omo-hyoids and upper part of the trapezii act in very forcible inspiration.

Next to the diaphragm, the intercostal muscles are the most important factor. They and the diaphragm are antagonists, although they concur to produce the same result. The rotation of the ribs, from the second downward, is accomplished solely by the intercostal muscles (Hoover). These muscles hypertrophy from overuse as in emphysema. The antagonism of the diaphragm and the intercostal muscles occurs as follows. When the line of traction and the plane of the diaphragm coincide, that is, when it is neither arched upward nor downward, the diaphragm overpowers the intercostal muscles and the costal margin is drawn toward the median line. But if the diaphragm is arched, either upward or downward, the intercostal muscles gain the upper hand, and the rib margin moves away from the median line during inspiration.

The preponderance of either the intercostals or the diaphragm depends not upon the height of the latter, but upon its curve and line of traction. Disturbances of the antagonism of the diaphragm and intercostal muscles give valuable clinical information. As Hoover has pointed out, these two antagonistic forces may be observed by the direction of movement and the comparative movements of the median and lateral portions of the costal margins on the two sides. The direction in which any portion of the costal margin may move is determined by the resultant of these two forces. One is the expression of the action of the intercostal muscles, which always widens the subcostal angle and spreads the hypochondria; the other force originates in activation of the diaphragm and always draws the costal margin toward the median line. When the resultant of these two forces causes narrowing of the subcostal angle, the subcardial or median portion of the diaphragm is less convex than normal. When the entire costal margin is drawn toward the median line, the entire phrenic leaf has lost a large part of its convexity. The movement of the costal margins has nothing to do with excursion of the diaphragm; it is merely the resultant of activation of the intercostal muscles and of the diaphragm. The only sign of phrenic excursion is protrusion of the epigastrium and lateral portions of the abdomen.

Methods of Examining the Diaphragm.—(1) The most accurate method is direct inspection by the fluoroscope. Examined in this way, the contour, the degree of movement and the presence of adhesions of the diaphragm may be accurately studied. (2) The roentgen-ray film will show the contour and the presence of deformities and adhesions. (3) The study of the excursion of the costal margins, with especial reference to the subcostal angle. This method, introduced by Hoover, is an excellent one. With the patient in the recumbent position, the examiner should place his thumbs symmetrically along the costal borders to serve as indicators, as inspection alone may lead to confusion between elevation of the thoracic cage and widening of the subcostal angle. In obese individuals the movements of the costal borders are usually obscured and can be

detected only by palpation. (4) By percussion of the lower border of the lungs, the excursion of the diaphragm may be made out quite satisfactorily. The lower limit of pulmonary resonance is first determined on the two sides with the patient breathing quietly. The patient then takes a deep breath and holds it. Normally, the pulmonary resonance should descend from $1\frac{1}{2}$ to 2 inches. If one of the leaflets of the diaphragm has become adherent at either of the angles, or has undergone interstitial changes, motion will be restricted or entirely absent on the affected side. If this is the case, there will be little or no change in the line of pulmonary resonance at the extreme base of the lung.

Litten's Sign (the diaphragmatic shadow, phrenic wave).—This sign is at times helpful in determining the motility of the diaphragm and the presence of pleural adhesions at the base of the chest. The sign is elicited by having the observer stand between a window and the patient or by placing the patient between himself and the window. The light should fall obliquely on the side under inspection. The patient is instructed to "breathe with his belly." As the abdomen rises and falls, a shadow will seem to move down the lateral aspect of the chest wall, between the sixth and the ninth ribs. During inspiration the diaphragm peels off from the chest wall, and by means of the negative pressure thus produced, causes the soft tissues to fall inward, so producing the shadow. Normally, this shadow has a range of from $2\frac{1}{2}$ to $3\frac{1}{2}$ inches, depending upon the depth of the respirations. The presence or absence and the extent of this shadow give one some idea as to the state of the leaflet on the affected side. The shadow is entirely absent if the diaphragm is adherent; it is diminished in cases of slight adhesions, pneumonia or a pleural effusion. The shadow is unaffected in subdiaphragmatic abscess.

It is difficult to elicit this sign in very obese subjects when the light is poor or the breathing is of the costal type.

Williams' Sign.—This is often noted in pulmonary tuberculosis, even when the lesion in the lung is slight. It consists of restriction of motion of the leaflet on the affected side. Several hypotheses have been advanced as to its causation. Adhesions of the pleura associated with the tuberculosis; impairment of pulmonary elasticity; irritation of the terminal fibres of the vagus; or involvement of the phrenic nerve on the affected side. This sign is best elicited by the fluoroscope.

SPASM OF THE DIAPHRAGM

The diaphragm may be subject to clonic or tonic spasms.

Hiccough.—This common condition is the most familiar example of clonic spasm of the diaphragm. It is the result of an intermittent or sudden spasm of the muscle. Hiccough is to be regarded as a reflex irritation, the source of which may be above or below the diaphragm. It frequently occurs in acute inflammatory lesions involving the abdominal viscera, as a postoperative condition following operations in the upper abdomen, in severe cases of typhoid fever, and occasionally with pericarditis. Hiccough and vomiting following abdominal wounds are always suggestive of injury to the diaphragm. Perhaps the most frequent cause

of hiccough is indigestion; the hiccough which so often occurs after a drinking bout belongs here. Hiccough is, at times, an annoying symptom caused by irritation of the central nervous system in cases of apoplexy, brain tumor or epilepsy; and it may occur, also, as a hysterical manifestation. In many instances there is no apparent cause for it.

Hiccough is produced in the larynx by the sudden inrush of air due to a sudden spasm and descent of the diaphragm. The glottis is taken unaware in a condition of incomplete dilatation (Fowler). The hiccough may occur at intervals of a minute or so, or it may occur so frequently as to interfere with breathing. If it continues for any length of time, pain is apt to develop along the line of attachment of the diaphragm to the chest. In the great majority of cases hiccough is a harmless symptom which lasts for a few minutes and then ceases. Occasionally, it may last indefinitely, even for months. Such cases are to be viewed with apprehension as death may result from exhaustion. In a terminal disease the occurrence of hiccough is to be regarded as an ominous sign and one which is the forerunner of death.

Paroxysmal sneezing, fits of laughing or weeping and coughing spasms, are of much the same nature as hiccough.

Tonic Spasm of the Diaphragm. Tonic spasm of the diaphragm is much less common than the clonic form. It occurs in tetanus, strychnine poisoning and hydrophobia. When the diaphragm is thrown into a tonic spasm there is a sense of constriction in the chest, intense dyspnoea and pain along the insertion of the diaphragm.

Epidemic Diaphragmatic Spasm.—In 1888 Dabney described a condition characterized by spasm of the diaphragm occurring in epidemic form. Within the past few years, similar small epidemics have been described under the name of "epidemic diaphragmatic spasm or 'Devil's Grippe.'" The clinical features are as follows: The attack nearly always begins suddenly, without prodromal symptoms. There is at first epigastric pain, which later extends to one or both ends of the lower thorax (the attachment of the diaphragm). Respiration is usually difficult and often rapid. In most cases the temperature rises at the onset and quickly reaches a maximum of from 101° to 106° F. Profuse perspiration is common. Nausea and vomiting occur in about one-third of the cases. In the beginning there is constipation but later diarrhoea occurs. In addition to the pain along the insertion of the diaphragm, there may be headache, pain in the lumbar region, shoulders and extremities. The paroxysms of pain and dyspnoea last from four to ten hours. The condition may be mistaken for acute abdominal disturbance but there is no shock and the pulse is slow and full. It may be mistaken for dengue but there is no rash and bone pains are absent. Its brief duration and diaphragmatic symptoms distinguish it from acute respiratory conditions. Torrey found that relief from the pain could be obtained by the use of quinine.

PARALYSIS OF THE DIAPHRAGM

Bilateral paralysis may be caused by either a central or a peripheral nerve lesion. Central lesions may be due to caries or fracture of the

cervical vertebræ, tumor of, or hemorrhages into, the spinal cord, progressive muscular atrophy, or myelitis. It often follows lesions of the peripheral nerves in which the phrenic nerves are primarily or secondarily involved. The most frequent cause of this form of paralysis is one of the acute infectious diseases, notably diphtheria, acute anterior poliomyelitis or Landry's paralysis. Diphtheria is probably the most frequent cause, although poliomyelitis has played a considerable role.

Bilateral paralysis is an extremely serious condition and may lead rapidly to a fatal termination. The signs and symptoms, as given by Fowler, are as follows: (1) Reversal of the respiratory movements of the epigastrium and hypochondria. These regions recede during inspiration instead of bulging. (2) Absence of downward movement of the abdominal viscera during inspiration. (3) Increased movement of the lower ribs. Owing to the paralysis of the diaphragm, the intercostal muscles are unopposed, and as a result there is widening of the subcostal angle and spreading of the hypochondria. (4) Dyspnœa on excitation or excitement. (5) Alteration in the character of the voice and cough. (6) Loss of the compressive action of the abdominal muscles upon the contained viscera, which ordinarily attends such acts as defecation and the commencement (but not the continuance) of urination. (7) Feebleness of expiration and of reflex respiratory actions as cough, sneezing and expectoration is a direct result of paralysis of the diaphragm. The presence of that condition prevents the previous inspiration from being sufficiently full to be followed by a forcible expiratory act. (8) Diminution of the total capacity of the thorax, owing to the increased arching of the diaphragm. The widening of the subcostal angle and the reversal of the movements of the epigastrium and hypochondria are typical signs of paralysis of the diaphragm. Fluoroscopic examination will show the absence of contraction of the leaflets and the abnormally high position of the arches. They may extend to the third rib or even higher.

Unilateral paralysis is of considerable clinical importance, as it is the most important contributing cause of massive collapse of one of the lower lobes of the lungs as a postoperative sequel. The diaphragm is the most direct and powerful expander of the lower lobes. If, therefore, as Pasteur originally pointed out, one of the leaflets is paralyzed as the result of traumatism during operative procedures in the upper abdomen, this powerful suction ceases or is inhibited, with the result that the lower lobe collapses. The symptoms and physical signs of this condition are considered elsewhere. In some instances Pasteur ascribed the collapse of the lung to reflex inhibition, caused by acute inflammation or acute pain in the neighborhood of the diaphragm. Unilateral paralysis may result, also, from a traumatic injury to the phrenic nerve on one side.

Unilateral lesions are never so severe as the bilateral. The severity of the symptoms varies considerably. Dyspnœa is usually present and the lower lobe of the affected lung may become congested, or there may be a localized bronchitis or bronchopneumonia. Paralysis of one of the leaflets of the diaphragm is to be suspected when respiratory symptoms and physical signs follow an injury along the course of one of the phrenic nerves. Fluoroscopic examination will show the arch on the affected side to be very high.

DIAPHRAGMITIS

Pathological changes in the muscle itself or its serous coats are of more frequent occurrence than is usually believed. The diaphragm is so frequently disregarded that there is available only a limited number of observations as to alterations in its structure.

Primary Diaphragmitis.—So far as we know at present, primary changes are unusual. The best-known example of primary inflammation of the diaphragm occurs in trichiniasis. The *Trichinella spiralis* frequently lodges in the muscle and may give rise to a serious myositis. Steiner¹ states that the diaphragm may be so extensively involved as to cause paralysis of the muscle and death.

In the terminal stages of scurvy there is often a brownish induration of the diaphragm or rupture of the muscle fibres and hemorrhage identical in nature with that occurring in the voluntary muscles. In these cases most intense dyspnoea and a feeling of constriction at the base of the chest may occur independently of any lesion in the lungs.

Secondary Diaphragmitis.—This is relatively common and may occur in association with inflammatory changes in either the thoracic or abdominal viscera. Changes secondary to involvement of the thoracic viscera are the most frequent. One obtains a fairly good idea of the frequency of the changes taking place in the diaphragm from a brief communication by Lucké.² In an analysis of 164 diaphragms, in which definite gross or microscopic lesions were found, Lucké found that in 68 the muscle showed various types of degenerative changes (hyaline degeneration, cloudy swelling, vacuolar degeneration, fatty degeneration, etc.); of special interest was a very marked fatty degeneration in cases of pernicious anemia. In 18 cases atrophy and fibrosis were found; most of the patients of this group were elderly. In 25 cases the diaphragm was the seat of acute inflammatory disturbance, which as a rule had spread from adjacent viscera. A number of cases in this group showed in addition degenerative alterations of the muscle fibres. Primary tumors were not encountered but in 17 instances metastasis had taken place. Tuberculosis of one or the other of the serous coats had occurred in 35 cases, and in a considerable number of this group tubercles were present in the muscle. In 9 cases of tuberculosis Allen J. Smith found miliary and conglomerate tubercles in all.

In pneumoconiosis changes in the diaphragm play an important part in the symptomatology. The dyspnoea, which is as a rule marked in the advanced stages of pneumoconiosis, is due partly to fibrosis in the lung, which interferes with its expansion, and partly to changes in the diaphragm itself. One or both leaflets may be adherent and in addition the muscle itself shows degenerative inflammatory changes due to the deposit of dust.

Most important contributions to the study of secondary involvement of the diaphragm are those by Pryor³ on the after-results of pleural effusion.

¹ *Boston Med. and Surg. Jour.*, 1908, **106**, 721.

² *Proc. Pathological Soc.*, Phila., 1924, **26**, 90.

³ *International Clinics*, vol. 2, 26th series, 1916, 94; *New York Med. Jour. and Med. Rec.*, 1923, **117**, 75.

He reported 146 cases and found that one individual in six escapes with the diaphragm unimpaired. Empyema is by far the most important factor in crippling the diaphragm. As a rule, one leaflet is involved but occasionally the condition is bilateral.

Morbid Anatomy.—The explanation as to why the diaphragm is so frequently involved secondarily is because of its rich lymphatic supply. Through these channels bacteria may be carried upward from the abdomen, or, more commonly, the infection arises from the lungs or pleura. In pleural effusion, particularly empyema, infection of the diaphragm is extremely common and only about one out of six escapes with the diaphragm unimpaired. In the case of effusions, the earliest change noted is a hyaline degeneration of the muscle fibres. This may be slight and result in no serious after-effects or it may progress and eventually lead to changes in which the muscle feels like a sodden, doughy mass of infiltrated tissue. It is also stiff, unyielding, and more or less thickened. Later, the muscle loses its elasticity, becomes rigid and atrophied, and finally, as the result of fibroid changes, hard and immovable. As a rule, the affected leaflet becomes fixed in the low, or below the middle position. An additional factor in producing injury in cases of effusion is the weight of the fluid as is especially true in cases of large empyemas. As a result of the loss of elasticity, due to the inflammatory changes and the weight of the fluid itself, the contour of the affected leaflet may be reversed, the convexity being toward the abdomen.

Another important factor in bringing about disturbance of the function of the diaphragm is the formation of adhesions. These may occur in one or both of the so-called angles or sulci (phreno-pericardial and phreno-costal). The phreno-costal sulcus is most often involved. As the latter is the most dependent portion of the pleural space, a small amount of fluid and sediment may persist, even when aspiration has been most complete. This tends to set up an inflammatory reaction, which leads to adherence of the diaphragm to the chest wall. As the result of the adhesions at either of these points, the diaphragm becomes fixed, loses its normal contour and has a more or less restricted movement.

In pneumoconiosis, adhesions at the angles are common. Varying degrees of myositis occur, and in addition, the contour of the diaphragm is often markedly deformed by sharp, angular projections. These sharp angulations are apparently the result of the diaphragm becoming attached to fibroid strands extending from the hilum of the lung to its periphery.

The heart may be drawn toward the middle line, and as a result of adhesions and traction, any assume the shape of a tube. According to Pryor, it differs from the dropped heart or atrophic heart sometimes seen in tuberculosis.

Symptoms.—The chief symptoms of immobility of the diaphragm, following inflammatory changes, are dyspnoea and soreness, or a sensation of dragging in the lower part of the chest, which may persist for a long time after absorption of the fluid. The dyspnoea occurs, as a rule, only on exertion. In tuberculous patients dyspnoea is, at times, marked and out of all proportion to the amount of pulmonary damage. On the other hand, many patients with extensive tuberculous lesions do not suffer

from dyspnoea. In the former it will be found that the diaphragm is usually at fault, while in the latter both leaflets move freely. In pneumoconiosis the dyspnoea is to be ascribed to two factors, extensive fibrosis of the lungs and a restricted movement of both leaflets. The dyspnoea may be aggravated by interference with the heart action. If the heart is markedly displaced or twisted as the result of adhesions, the dyspnoea may be extreme.

Physical Signs.—Restriction of the movement of the diaphragm is seen in its most characteristic form in two conditions, namely, following a pleural effusion and in pneumoconiosis. With inflammatory effusions, the diaphragm may escape if the fluid is rapidly absorbed or removed shortly after it has accumulated. If, however, the effusion has been present for some time, especially an empyema, evidences of diaphragmatic disturbances are almost certain to be found. In such cases physical signs persist at the base of the affected chest in spite of the removal of a large amount of fluid. These signs have usually been ascribed to the fact that the lung had failed to expand. In a sense this is true but the real cause has been the disablement of the diaphragm which may be partially or completely incapacitated. If such is the case, the greatest factor in the expansion of the lower portion of the lung is interfered with. The physical signs under these circumstances are absence of Litten's sign, restriction of motion, dulness on percussion and distant or suppressed breath sounds.

The most certain method of determining the function of the diaphragm following pleural effusions is by fluoroscopic examination. The restoration to normal of the structures at the affected base depends largely on the character of the fluid and the length of time it has remained in the chest. When the damage to the diaphragm has been trivial, there is a final return to normal. In other cases a fair degree of motility takes place after months. In still others the injury is permanent and the affected base will always show abnormal signs. Furthermore, as a result of poor ventilation of the affected side, acute inspiratory infections involving that portion are common.

Treatment.—This is largely preventive, especially in the case of purulent effusions. Unless the purulent fluid is tuberculous in origin, it should be dealt with surgically and drained at the most dependent portion. Serous effusions, if large, should be tapped; small ones are usually ignored. Unless the patient is tuberculous, breathing exercises to aid in the expansion of the lung and increase the motility of the affected leaflet are desirable.

DIAPHRAGMATIC HERNIA

The term diaphragmatic hernia is loosely applied to any condition in which the abdominal contents protrude through the diaphragm into the thoracic cavity. The term should be restricted, however, to those instances in which the abdominal viscera are enclosed in a sac composed of all or one of the component layers of the diaphragm. In the great majority of instances a true diaphragmatic hernia is congenital. Those instances in which, as the result of a stab wound or other traumatic

injury, a rent is made in the diaphragm, should be considered as examples of evisceration or spurious hernia.

Diaphragmatic hernia may be congenital or acquired. The former is considered to be the most common. Rolleston, however, is of the opinion that in not a few cases what is thought to be congenital hernia is in reality an acquired defect due to a forgotten injury received in the past.

Congenital diaphragmatic hernia is a developmental defect. In the early stages of the embryo the pleural and peritoneal cavities are continuous. At a later stage they are separated by a thin membrane which extends between the lungs and the Wolffian bodies. This thin membrane constitutes the beginning of the diaphragm and its development may be arrested in whole or in part. If the defect is extreme in character, the condition is incompatible with life and children so constituted are still-born. Extensive defects of this nature are usually associated with other developmental deformities. Rarely an individual born with a marked diaphragmatic defect reaches adult life. Instances are on record in which an entire leaflet has been wanting. Small defects, on the other hand, may cause no disturbance and, as a rule, are accidental discoveries. In addition to absence of all or part of one leaflet, the defect may consist of a localized bulging or pouching due to a weakness in the muscle near the œsophagus or xiphoid cartilage. A defect of this nature is probably the result of an inherent weakness at these points, plus severe straining.

A *true hernia* of the diaphragm may be acquired as the result of an injury which weakens or tears the muscle or its covering sufficiently to allow some of the abdominal contents to bulge into the thorax. True diaphragmatic hernia occurs more commonly on the left side than the right in the proportion of about $2\frac{1}{2}$ to 1. This type of hernia rarely gives rise to symptoms. The physical signs are similar to those in the traumatic type, and are described under that heading.

EVISCERATION (TRAUMATIC HERNIA, FALSE HERNIA, HERNIA SPURIA)

Etiology.—Evisceration is encountered far more frequently among men than women because the former are more exposed to traumatic injuries. Evisceration is almost exclusively a left-sided condition; over 90 per cent. of the cases reported being on that side. Eppinger, in an analysis of 561 cases of false hernia, found that the left side was involved in 527, or 95.6 per cent., while but 34, or 4.4 per cent. occurred on the right side. The most common cause of this type of hernia is a stab wound and Green reported 129 cases due to this cause. The frequency of stab wounds as a cause and the preponderance of left-sided lesions are explained as follows. The wound is usually inflicted by a right-handed person striking at the most vital and accessible part of his opponent, namely, the left side. In the second place, even if the right leaflet is injured, the liver acts as a plug. Occasionally, however, a portion of the liver may protrude through the opening and become strangulated. Gun-shot wounds, or wounds produced by exploding shells, may in like manner injure the diaphragm. In civil life, next to stab wounds, the diaphragm

may be injured by a severe strain, or, more commonly, by a crushing accident. In this latter group there is rarely any external injury.

Symptoms.—A traumatic injury to the diaphragm may be so severe as to produce death from shock immediately. If the patient survives, severe dyspnoea as a rule ensues immediately but it may be a late manifestation. Pain is not a marked feature but a feeling of constriction is common. Vomiting and hiccough are the most important symptoms, especially when the injury is on the left side. In the case of perforation with a small bullet, symptoms referable to the diaphragm are not usual, but if, instead of perforating directly, it causes a slit in the muscle, the respirations may be shallow, frequent and accompanied by a groan and slight hiccough on respiration. Varying degrees of pleuritis or peritonitis, or both, may follow the injury. If the damage to the diaphragm is slight and the patient survives, recovery from the initial shock takes place and the patient may suffer no inconvenience. If, however, there is protrusion of the viscera into the thorax, an irritating cough is apt to occur, dyspnoea is marked on exertion, and there is pain in the lower left chest. In addition to the respiratory symptoms, the digestive organs are disturbed and the patient complains of colicky pains, constipation and vomiting. Emaciation as the result of disturbed nutrition usually occurs.

Physical Signs.—With few exceptions the physical signs are limited to the left side. *Inspection.* The presence of a wound in the lower left side is of great importance. If associated with hiccough, vomiting and dyspnoea, injury to the diaphragm is almost certainly present. In stab wounds a portion of the omentum often protrudes through the external wound. It may be noted, also, that the abdomen is flattened and the lower part of the chest is distended. If the rent in the diaphragm is large and allows the abdominal viscera to pass through, bulging of the chest and displacement of the heart upward and to the right may be marked. Expansion of the left lung is usually diminished. *Palpation.* Over the lower part of the left chest fremitus is absent and the maximum impulse of the heart is felt to the right of its normal position. *Percussion.* On the left side the percussion note is usually tympanitic, due to the underlying stomach and intestines, but in some instances protrusion of the spleen or the presence of a hemothorax may give a dull or flat note. Rarely when large amounts of intestine enter the thorax the tympanitic note may extend to the right side, in which case there will be pulmonary resonance above, then tympany and liver dullness below. *Auscultation.* The breath and voice sounds are absent, except along the spine and in the upper chest. Gurgling sounds are usually heard due to the movement of flatus or fluid in the stomach or intestines.

The *roentgen-ray examination* clinches the diagnosis. With the fluoroscope, the normal dome-like contour of the leaflet is seen to be irregular in outline, being blurred at some points and clear at others. Motion is impaired or absent, or there is a reversal of the normal respiratory movement. If bismuth is given, the dome becomes very irregular in outline from the shadows produced by the displaced stomach and intestines. If the stomach is distended, it may be seen high up in the thorax with lung shadows showing through it.

Diagnosis.—In the absence of an external wound, the condition may be mistaken for a pneumothorax. In evisceration there is abdominal flattening and the presence of gurgling sounds produced in the prolapsed stomach and intestines. In pneumothorax there may be bulging of the intercostal spaces. In both conditions there is restriction of motion, distant or absent breath sounds, and displacement of the heart. The characteristic signs of pneumothorax, namely, the succussion splash and the coin test, are absent in evisceration. The roentgen-ray examination will distinguish conclusively between the two conditions.

EVENTRATION OF THE DIAPHRAGM

The reported instances of this condition are comparatively few. It is almost invariably an accidental discovery, and doubtless many individuals who have it never undergo the examinations necessary to determine its presence. Eventration is a condition in which one leaflet of the diaphragm although intact, is unduly expanded, and thus reaches an abnormally high position. As a result, the abdominal viscera are displaced upward into the thoracic cavity. In both true and false hernia there is either an abdominal bulging or a definite opening in the muscle. In eventration the leaflet is intact and the contour is regular. In addition to the term "eventration," the condition has been referred to as insufficiency, relaxation, dilatation or elevation of the diaphragm.

Etiology.—The abnormality is ascribed to one of two causes. (1) That it results from increased abdominal tension. Against this are the following facts. It is more common in men than in women, although the latter may have passed through a number of pregnancies. Then, too, it is at times encountered in infants and young children. (2) That eventration is a congenital abnormality seems apparent from the following facts. It occurs in infants, the affected lung is not compressed, and there is no history in these cases of traumatism or acute infection that might lead to weakness or elevation of the diaphragm. Bayne-Jones¹ collected 45 cases from the literature. The great majority occurred in males. It is almost invariably on the left side; in only 3 of the above series was the right side involved.

Symptoms.—As the condition is congenital, both the thoracic and abdominal viscera accommodate themselves to the defect and as a result there are no symptoms. The condition may be suspected on physical examination, but in most instances it is discovered as the result of roentgen-ray examination or at the autopsy table.

Physical Signs.—In the left-sided cases the most striking sign is an abnormally large area of tympany both anteriorly and posteriorly. Over this area the breath sounds are absent and there may be gurgling sounds due to the movement of fluid in the stomach or gas in the intestines. The lung is not compressed but the heart may be displaced upward or to the right. The condition is definitely shown by the roentgen-rays. The contour of the left leaflet of the diaphragm is that of a smooth, sharply-defined, bow-shaped shadow with a bright area below and the

¹ *Arch. Int. Med.*, 1916, 17, 221.

lung shadows above. If bismuth be given the stomach and intestines form new shadows.

Of the 3 reported cases on the right side, only 1 was recognized during life (Bayne-Jones). In this case there was absence of Litten's shadow and dullness and absent breath sounds between the third and fifth ribs. Above the dull area there was pulmonary resonance and below it tympany. Inflation of the colon displaced the dull area upward and increased the area of tympany.

Diagnosis.—Owing to the large area of tympany, the conditions most likely to simulate eventration are pneumothorax or congenital hernia. Among the more unusual conditions are a large basal cavity, subphrenic abscess producing gas and paralysis of the diaphragm. The essential feature of eventration is that it is not associated with any symptoms, while all of the conditions mentioned are, with the possible exception of a latent pneumothorax, productive of symptoms. In the case of latent pneumothorax evidences of tuberculosis are usually present. Furthermore, in spontaneous, non-tuberculous pneumothorax there is marked displacement of the heart, and there may be a positive coin test, which is never present in eventration.

A large basal cavity is associated with other signs of thoracic damage. In subphrenic abscess there are, in addition to the abnormal physical signs, the constitutional disturbances commonly occurring in septic cases. Paralysis of the diaphragm is either associated with a traumatic injury or one of the acute infections. Hernia and evisceration both cause marked changes in the thoracic viscera, such as displacement of the heart and compression of the lung. Evisceration is always secondary to a traumatic injury.

Treatment.—As eventration never gives rise to any disturbance and is usually an accidental discovery, it requires no treatment.

PART II

DISEASES OF THE CIRCULATORY SYSTEM

CHAPTER XII

GENERAL CONSIDERATIONS IN CARDIOVASCULAR DISEASE

By CHARLES F. HOOVER M.D.

Introduction.—The problem for a physician to solve when confronted with a case of circulatory disease is, which of the many factors in the maintenance of the circulation are at fault? Briefly stated, he must determine if there is a faulty distribution of the blood, viz., in the peripheral vessels, in the splanchnic area or in the pulmonary circulation; if the pure hydraulics of the circulation are maintained and if its accomplishment is fulfilled without an expenditure of more than a normal amount of work by the heart. Some of these problems have their solution in phenomena purely physiological, some pathological, and some are still in the realm of theoretical speculation. Where physiology and pathology fail, the diagnostician can appeal only to recorded clinical symptomatology.

The factors in the normal maintenance of the circulation are: An efficient myocardium with a sound directing innervation, efficient and unobstructing valves at the atrioventricular and arterial orifices, an aorta and branches of suitable calibre with elastic walls. Furthermore, the aortic system must fade into small branches with walls of given elasticity and vasomotor tone. There must be an unhindered centripetal flow of blood in the veins, supported by the vasomotor tone of the venous walls and valves and contraction of the skeletal muscles.

We have not only the propelling agencies to consider, but also the aspirating forces in the thorax. These are the normal negative tension in the pleural cavity and the inspiratory effort in breathing. Another aspirating force is from the diastole of the heart, which may have some importance; in some instances of pericardial and myocardial disease a faulty diastole may be the chief cause of trouble. The problems mentioned have to do largely with the systemic circulation and most circulatory disturbances occur in this distribution, but the right ventricle and the pulmonary vessels may be the seat of trouble which is primarily in the pulmonary arteries or induced secondarily from diseases of the lung.

This discussion will be restricted to the consideration of a few of the physiological aspects of diseases of the circulation, and an attempt to

show that this view of cardiovascular disease may engage the attention of a physician without the aid of any so-called instruments of precision.

Distribution of Blood.—If the equable distribution of blood be disturbed, the cause must be in the central pumping organ or somewhere in the systemic or pulmonary vascular system. The most direct method of determining the site and character of the defect is to locate, if possible, a point where massing of the blood occurs. Massing of the blood at the proximal side of a lesion is often the source of symptoms which most attract the patient's attention, viz., cough and dyspnoea from pulmonary stasis, when the left side of the heart is the seat of trouble; or discomfort in the hepatic region from stasis in the liver when the right heart is no longer able to propel a sufficient mass of blood. When propulsion of blood in the distal circulation is impaired, evidences of the character above mentioned are notably absent and the mass of blood accumulates in the splanchnic circulation, as seen in shock, depressor nerve influences and vasomotor exhaustion in the terminal stages of infectious diseases. The same occurs in instances of reflex vasomotor dilatation in the abdominal vessels.

If there is impairment in mass movement of the blood, either of a positive or negative character, the first duty of the physician is to seek some evidences of an excessive accumulation which may be under increased pressure or under diminished resistance of the sustaining vascular walls. Dilatation of the splanchnic vessels is a common instance of the last-named condition. Stasis in the pulmonary circulation is by far the most common evidence of excessive accumulation of blood when there is any pure hydraulic distress in the cardiovascular system. Primary disease of the pulmonary arterial system is rare. Although the branches of the pulmonary artery have an abundant supply of muscular tissue in their walls, there is a very feeble vasomotor nerve supply. In the pulmonary circulation there is not the same demand for widely varying degrees of resistance in certain regions of supply, as in the aortic system. The respiratory function at any given time is the same in all parts of the lung; so there is no need of any device which will increase the supply to one portion of the lung over that of another part. What role vasomotor impulse plays in the pulmonary circulation is unsolved. Experimentally, no one has succeeded in demonstrating a rise of pressure from vasoconstriction of more than about 20 per cent. of the normal pulmonary arterial pressure.

Blood Hydraulics.—To make an adequate examination of the heart the physician's attention must be directed to answering the questions as to whether the volume blood flow is defective or not, and also if the circulation is maintained with any changes in the size of the heart's chambers or alterations in the musculature.

One of the most finished accomplishments in physical diagnosis is to define the outline of the heart in its superior, lateral and inferior borders and to resolve the whole area into its component parts; by which is meant to differentiate between enlargements of the heart and its sac, and to determine which part of the precordial area belongs to the right auricle and to the right and left ventricles.

Although modern instruments of precision, like the roentgen-ray and electrocardiograph, give great assistance in determining the heart's size and its auriculo-ventricular mechanism, still the final clinical judgment rests literally in the hands of the examiner. For the roentgen-ray gives accurately the outline of the pericardial sac in its upper and lateral borders, but it fails to outline the inferior border of the heart within the pericardial sac. The contour of the ventral aspect of the heart can be inferred only from signs that reveal the degree of convexity of the subcardial diaphragm. The analysis of the precordial area can be made by direct physical examination only. The electrocardiograph accurately pictures the time of activation of the auricles and ventricles, but it reveals no information about the vigor or reserve energy or output of the heart.

The pulse can be adequately examined by the fingers only. No instrument will trace the excursion of the artery, its systolic and diastolic filling or the character of the anacrotus and the katarotus. All instrumental pulse tracings must be guided by the criticism of touch. In former years the "tactus eruditus" was the boast of physicians. In recent times it is less cultivated because the systolic and diastolic pressures can be measured by the sphygmomanometer, and this important observation has quite obscured the importance of the "learned touch" which should be more diligently cultivated to procure safe criticism in the use of the instrument.

Pressure can be accurately estimated by the fingers if a large artery is used like the femoral which is covered by thin integument and lies against the firm surface of the pubic bone. If the artery is compressed, and by means of a stethoscope the amount of pressure needed entirely to shut off the arterial flow is determined, it will be found by a little practice that one's digital estimation will conform very closely to that made by the instrument. When the two methods give widely different results further investigation will often show the instrumental measurement to be undependable.

A large artery with unvarying calibre serves the manual method because what we palpate is not the abstract factor of pressure, but the concrete phenomenon of pressure associated with area. We palpate bursting tension which is equal to pressure multiplied by the diameter of a vessel. Therefore the artery with a large unvarying calibre is preferable to the small artery which alters its calibre with varying vasomotor tone. The advantage in employing a large artery is comparable with the advantage of a lens of high power over a low power lens, for in the larger artery we have a greater multiplier of the pressure to furnish the bursting tension. For recording purposes the instrument should be used, but its use should always be subjected to the criticism of the fingers. As instruments of precision multiply, our methods of bedside examination should grow in accuracy for if they do not we soon become witless servants of our instruments.

Estimation of the Heart's Volume.—In making a physical examination of the heart one should always endeavor to get a definite idea of what proportion of each of the three chambers contribute to the precordial area. The left auricle cannot be estimated with satisfactory accuracy,

but we can always gain a definite idea about the areas of the two ventricles and the right auricle and arch of the aorta as they are projected on the anterior thoracic wall.

This subject is discussed in detail because in recent times some very competent authorities have expressed scepticism on the accuracy of percussion of the heart's borders. This scepticism has arisen from two sources. The infallibility of the six-foot roentgen-ray plate for measuring the frontal projection of the pericardium has caused waning interest in the art of percussion. The direct palpation percussion gives very accurate results in defining the upper and left and right borders of the heart. Sometimes the conformation of the thoracic wall and intra-thoracic complications, such as exudative pleurisy and tumors, may interfere but in most cases the frontal projection of the heart can be accurately defined by direct percussion. Mediate percussion is particularly incompetent for defining the right heart border, for when the thoracic wall is fixed by the pleximeter finger and struck by the hammer finger a large surrounding area of the thoracic wall is set in vibration which gives a resonant note from aëreated lung to the right of the heart. It is like etching a fine border with a large blunt instrument. To define the heart's borders one should employ a small penetrating pleximeter. Otherwise the definition between the heart's border and adjacent lung will be lost. The end of the extended finger should be used. If the finger is flexed the muscular sense of the long and short finger flexors is obscured. It is like percussing with a frozen finger. To preserve the muscular sense in the flexors of the finger the muscles should not be in a state of contraction.

To percuss the heart with accuracy the patient should be upright. In the dorsal position the heart's borders cannot be accurately defined because the heart then recedes from the anterior chest wall. Neither the lateral nor the posterior projections of the heart are accessible to physical examination, but the inferior or ventral aspect of the heart does lend itself to analysis by physical examination. The nest of the diaphragm hides the inferior boundary of the heart from the frontal roentgen-ray plate, but by gaining some evidence for flattening of the subcardial diaphragm we can gain a very clear conception of the convexity of the ventral surface of the heart to the left and to the right of the median line. When the subcardial diaphragm is flattened by cardiac or pericardial enlargement the inner halves of both costal margins move mediad with inspiration, *i. e.*, there is inspiratory narrowing of the subcostal angle as the lateral portions of the costal borders move laterad.

When only the left side of the heart is enlarged the subcardial diaphragm to the left of the median line is flattened and then the left costal border from the median line to the end of the eighth rib is either restrained during inspiration in its lateral movement or if the flattening is sufficient the inspiratory movement is mediad. When only the right ventricle and right auricle are enlarged, as often occurs in acute phosgene poisoning, the same change in the extent and in the direction of movement is seen in the right costal border from the median line to the end of the right eighth rib.

This method of estimating cardiac enlargement is very serviceable in

examining patients in the dorsal position. To make the observation the patient should be lying down with all the abdominal muscles relaxed for otherwise the recti and transverse and oblique muscles come into play by their restraint to movements of the thoracic cage. The phrenic and intercostal muscular control of extent and direction of movement of the inner portions of the costal borders is so delicately balanced that very moderate flattening of the subcardial diaphragm serves to modify the normal inspiratory widening of the subcostal angle.

By this method of studying evidence for changes in the ventral convexity of the heart, cardiac enlargement can be readily detected in the dorsal position when it cannot be detected by percussion. This method also aids in studying changes in the heart's enlargement under therapy. When first observed the enlarged heart may cause inspiratory narrowing of the subcostal angle and then as under therapy the right ventricle and auricle diminish in size the inner right costal border ceases to move mediad and resumes its lateral movement with inspiration. If the left heart remains permanently enlarged the inner half of the left costal border will continue to move mediad or if the left side of the heart diminishes also, the left inner costal border may move weakly laterad and if the heart returns to its normal size the subcostal angle resumes its symmetrical inspiratory widening.

This alteration of movement in the subcostal angle in cardiac enlargement occurs only in cardiectasis and not in enlargements of the heart that are compensatory for an increased mass movement of blood, as occurs in early Graves' disease, in arterio-venous fistula and in congenital heart disease in which the heart is still capable of maintaining a sufficient output. The inspiratory movement of the subcostal angle affords a very accurate method for estimating the amount of fluid in the pericardial sac and also provides a very delicate method for estimating changes in the amount of pericardial fluid in pericarditis. By aspirating fluid from the pericardium I have often observed the gradual transition from strong inspiratory narrowing to widening of the subcostal angle as the amount of fluid in the sac diminished.

Analysis of the Precordial Area.—After the dimensions of the precordial area are determined, the portions that belong to each ventricle and the right auricle should be defined. When the left ventricle contributes to an increased cardiac area its impulse is circumscribed and can be differentiated on the mesial side from the broad quadrilateral area of impulse from the right ventricle which may extend from the right border of the sternum to the left mid-clavicular line and in extreme cases even further laterad. The enlargement of the precordial area to the right of the sternum is due either to enlargement of the pericardial sac or the right auricle. The right ventricle is very rarely enlarged to the right of the sternum. There may be a very considerable increase of the size of the right ventricle and the precordial area not extend beyond the left mid-clavicular line. This is often true in pronounced mitral stenosis and may lead to an underestimate of the size of the ventricle.

In this relation it should be remembered that the right may with equal accuracy be called the anterior ventricle. To gain a conception of its

increased size we are left to estimate the vigor of the forward thrust of the ventricle. This appreciation of the increased impulse of the right heart is more clearly gained by applying the ear directly over the heart. If the impulse is palpated manually the forward thrust is perceived by the muscular sense in the thoraco-scapular muscles and the muscles of the arm and forearm, whereas when the head is applied over the precordium the impulse is perceived by the adjusters of the head position. Enlargement of the right auricle to the right of the sternum occupies a semilunar area which has its upper limit at the third and the lower limit in the fifth interspace. All enlargement of the heart to the right of the sternum can be safely reckoned as due to the right auricle.

Whether the left auricle is enlarged or not can be logically deduced from the demonstrable areas of the other three chambers. The volume of each chamber of the heart should be evaluated before any sequential relation between disease of the left and right sides of the heart can be established, or for that matter before any clear conception can be formed about resistance to outflow from either ventricle or leakage of a valve. Such a point of view is essential to differentiate between some defect in the hydraulic blood flow and a primary disease of the heart muscle. The volumes of all the chambers should be defined if a differentiation is to be made between enlargements of the ventricles due to an increased volume flow, as occurs in Graves' disease, and cardiectasis due to myocardial disease.

There may be considerable enlargement of the left heart without increase of the precordial dulness to the left. This does not occur in any disease that causes either a compensatory increase in the volume of the cavity of the left ventricle or that may cause cardiectasis. When, however, the left ventricle is hypertrophied secondarily to an elevation in blood-pressure the increase in the periphery of the ventricular wall may not increase the lateral extent of its frontal projection and therefore the left border of the heart in the fourth and fifth interspaces is not beyond the mid-clavicular line. The right ventricle and auricle are unaffected, consequently percussion and palpation do not reveal any evidence for the enlargement of the left ventricle. If the inspiratory widening of the subcostal angle is studied the inner half of the left costal border will be found to move laterad with much less vigor than the right border and also the extent of movement is lessened. This restraint in lateral movement of the left costal border is due to flattening of the subcardial diaphragm to the left of the median line and it is the only physical sign under these conditions that provides direct evidence of enlargement of the left ventricle.

This kind of enlargement of the left ventricle cannot be accurately portrayed by the roentgen-ray because the left is just as much a posterior as the right is an anterior ventricle so that a frontal projection of the heart fails to give evidence of an increase in the heart's antero-posterior dimension and neither does the roentgen-ray silhouette of the heart define its extent in a ventral direction. This portion of the heart is hidden in the nest of the diaphragm and its increase in size can be detected only by recognizing the consequent flattening of the left subcardial diaphragm.

In acute phosgene poisoning we may have a similar condition that

affects only the right heart and does not include the left ventricle or auricle. On account of the abundant thrombi in the pulmonary circulation the right ventricle and auricle dilate, but owing to the severe pulmonary œdema and acute emphysema which accompany the trouble the enlargement of the right auricle to the right of the sternum is obscured to percussion. The subcardial diaphragm, however, is flattened to the right of the median line by ectasis of the right heart and consequently the inner half of the right costal border is restrained in its lateral movement with inspiration or may move mediad while the symmetrical part of the left costal border moves laterad. I have often in this way detected an acute dilatation of the right heart when there was no other physical sign to betray it.

Cardiac Enlargement Due to Increased Volume Flow.—There are two very notable conditions in which the ventricles are enlarged as a compensatory measure to accommodate an increased volume flow of blood. The one, Graves' disease, is very common, the other, arterio-venous fistula, is very uncommon. In both diseases the auricles are not enlarged, but the capacity of the two ventricles is increased and so is the diastolic-systolic excursion which often misleads the examiner to over-estimate the size of the ventricles, because the vigor of the forward thrust of the heart carries with it an area of the thoracic wall that is larger than the silhouette of the heart and therefore accurate percussion and the roentgen-ray both reveal the heart as smaller than the breadth of the impulse indicates it to be.

In the early period of Graves' disease when the heart is enlarged to accommodate its increased output and when there is no stasis in the circulation the percussion area may be much enlarged, but the subcardial diaphragm is not flattened as it would be were the same degree of enlargement caused by ectasis with decompensation. Later in the course, when the heart becomes incompetent, its size may not be demonstrably larger, but the subcardial diaphragm then is depressed and reveals an impairment in the inspiratory widening of the subcostal angle.

A very similar state of affairs exists in cardiac enlargement secondary to a large arterio-venous fistula. The two ventricles are much enlarged, but the right auricle is not enlarged although there may be a very strong systolic hepatic pulse. The precordial impulse is very large and includes the whole area of the right as well as the apex of the left ventricle. If the fistula is closed by the examiner's finger, the precordial impulse is immediately diminished in extent. The area of the right ventricle ceases to be included and only the apex of the left ventricle supplies a source for the precordial impulse. Just as in Graves' disease, the subcardial diaphragm is not flattened, although an equal enlargement of the precordial area due to primary disease of the myocardium would give very marked signs of flattening of the subcardial diaphragm.

This point of view on cardiac enlargement and the resolution of the precordial area into its component parts, viz., the two ventricles and the right auricle can be attained only by direct physical examination and cannot be accomplished by means of any instrument of precision.

The Evaluation of Several Signs of Stasis.—It is not only pulmonary œdema and lung rigidity with retention of body fluid that may be wrongly estimated as measures of failing circulation, but there are some physical signs associated with heart disease that may be very deceptive and can readily mislead an examiner in appraising the degree of cardiac incompetence. The area of hepatic percussion dulness, the position of the lower liver border and systolic pulsation of the liver may at times be very misleading.

Hepatic Displacement.—No intra-thoracic disease causes such hepatic displacement as enlargement of the heart or pericardial sac. Pericarditis with effusion that is not very large may displace the liver to a surprising extent; 200 c.c. of pericardial fluid may displace the liver border as far as four fingers breadth below the costal border. It is not uncommon for hepatic displacement to be mistaken for hepatic tumor or abscess.

One such instance occurred in a patient with pneumococcus pericarditis in whom the lower border of the liver in the nipple line was on a level with the anterior-superior spines of the ilium. After the withdrawal of 700 c.c. of sero-purulent fluid from the pericardial sac the liver rose to its normal position. Whenever there is sufficient fluid in the pericardial sac to cause cardiac embarrassment the hepatic displacement is very pronounced unless there should be a synechia between the epicardium and pericardium on the inferior aspect of the heart.

This degree of hepatic displacement is due to the fact that the pericardial sac is fixed in the mediastinum and the subcardial diaphragm is displaced by the enlarged pericardial sac which covers the upper and posterior as well as the anterior part of the diaphragm. The liver cannot be displaced *in toto* but is rotated on a transverse axis that is furnished by that part of the liver which is uncovered by peritoneum. This part is the quadrilateral area on its posterior aspect that is bounded by the reflections of the peritoneum from the upper and lower surfaces of the liver to the posterior abdominal wall. Downward displacement of the diaphragm in its posterior subcardial portion is attended with a downward rotation of the liver which is magnified at the liver border just as the distance of movement of the weight in a lever of the third class is a magnification of the distance of movement of the power. So the further posteriorly in the subcardial diaphragm a given amount of ventral displacement is located the greater will be the displacement of the anterior hepatic border in a downward direction.

Such a rotation of a liver on its posteriorly placed transverse axis causes the convex hepatic surface to present itself as a transversely placed convexity of the abdominal wall with a sella between the right costal border and the liver protrusion. And what contributes still further to deception in this phenomenon is inaccessibility of the hepatic edge which is rotated downward and in a posterior direction away from the anterior abdominal wall. Consequently the hepatic edge is not palpable and there is a depression between the dome of the upper liver surface and the right costal border that simulates an abdominal tumor below the costal margin.

It is not uncommon to estimate the more moderate displacements of

the liver that occur in enlargement of the right side of the heart as hepatic enlargement from stasis. This is particularly true in cardiac enlargements from synechia cordis and mitral stenosis, diseases in which the right heart is particularly enlarged. Enlargement from stasis will not obscure the hepatic edge. This is shown in obstruction of the hepatic veins without cardiac disease. The downward rotation of the liver edge should always indicate displacement to be the cause of appearance of the liver below the costal border.

The palpable liver systolic pulse may lead one to greatly exaggerate its significance for hydraulic failure of the circulation. One source for this deception lies in the fact that a regurgitant pulse by way of the hepatic veins distends Glisson's capsule just as it would were the hepatic veins in communication with a great volume of blood contained within the liver capsule as a single reservoir, instead of being subdivided into a great number of small channels like the hepatic veins. It is like a great venous aneurism with a diameter as great as that of the liver. What we palpate is the bursting tension on Glisson's capsule. The bursting tension on the walls of a vessel is measured by multiplying the pressure by the diameter of the vessel (*e. g.*, $P \times 2 R$ or pressure times twice the radius). Consequently if the pressure is the same in two hydraulic chambers one of which has a diameter thirty times greater than the other, the bursting tension in the larger chamber will be thirty times greater than in the smaller. What we palpate is the concrete phenomenon of bursting tension and not the abstract phenomenon of pressure. By touch we cannot estimate pressure apart from the factor of area. We are often surprised to see a regurgitant systolic pulse in the bulbus venosus or in the internal jugular vein when there is none in the liver, and conversely we may palpate a strong pulse in the liver when no pulse is visible or palpable in the cervical veins. To approximately estimate the significance of these hepatic and venous phenomena on the proximal side of the right heart as evidence for cardiac incompetence we should test the lung extensibility and the proportion between the heat loss from the lung and the body surface.

Air Hunger and Cyanosis.—In failing circulation air hunger always precedes cyanosis. There may be great air hunger with cyanosis and cool body surface when the cyanosis is purely peripheral and when there is no anoxemia in the aortic blood. Aortic anoxemia does not occur until there is abundant interference with the transpiration of gases between the ventilating air and circulating blood on account of pulmonary edema. But when the patient has air hunger in failing blood hydraulics and the alveolar air has a normal content of both oxygen and carbon dioxide and the arterial blood is sufficiently rich in oxygen the storage of oxygen in the tissues will be reduced by a defective blood flow just as it is reduced by violent exercises when there is an increased demand for oxygen by muscular work. The working athlete is not cyanotic, the oxygen saturation of the blood is normal and the alveolar air has a low carbon dioxide and high oxygen content, but there is intense air hunger while exercise is performed which persists for a considerable time after work ceases until the storage of oxygen in the tissues is restored to its normal amount.

So in the patient with failing blood flow, air hunger exists without cyanosis because the supply of oxygen to the body structures is defective although the chemistry of the ventilating air and arterial blood is quite normal.

Hippocratic Finger Nails.—When a patient with cardiac disease is found with drum-stick finger ends we may be quite sure that this sign of aortic anoxemia is not a measure of failing output of the left ventricle, but must be due to an admixture of venous with arterial blood from congenital heart malformation or from defective ventilation in a part of the lung that still has considerable blood flow. These are the only two ways in which there can be enough aortic anoxemia to suffice for the production of drum-stick finger ends. How are we to know if cyanosis of the fingers is due to aortic or peripheral anoxemia? Simply by observing the temperature of the fingers. Warm cyanotic fingers must be due to aortic anoxemia. When the fingers are cold and cyanotic the anoxemia is either purely peripheral or may, of course, be combined with aortic anoxemia.

It is quite obvious that a cyanotic body surface which is warm must have an abundant blood supply and if it is warm and cyanotic there must be an abundant supply of arterial blood that has reduced hemoglobin. The cyanosis from methemoglobin looks exactly like that from reduced hemoglobin. How are we to differentiate between the two? Simply draw a drop of blood and catch it with blotting paper. Methemoglobinemia that simulates anoxemia will yield a chocolate colored blood that retains its dark color after exposure to the air, but the cyanosis due to anoxemia yields a dark blood that will speedily take on the color of oxyhemoglobin after it is spread on the blotting paper.

When air hunger with cyanosis occurs in cardio-respiratory distress there may be some difficulty in evaluating the parts played by circulatory failure and respiratory defects. If there is an enlarged heart, air hunger and cyanosis with much moisture in the air spaces, and also drum-stick finger ends, we are in all probability dealing with an old bronchitis and emphysema that has finally resulted in cardiac dilatation from chronic anoxemia.

When cardiac dilatation occurs in chronic emphysema the left and right ventricles are equally affected. I have never seen dilatation of the right heart as a result of emphysema without dilatation of the left also. My clinical experience does not confirm a current opinion that right ventricular dilatation is caused by obstruction of the vascular area in emphysema. Should the bronchitis and emphysema be due to sclerosis of the pulmonary arteries then, of course, we see dilatation of the right without dilatation of the left heart. Another cause of dilatation of the right ventricle and right auricle that I have seen accompanying chronic bronchitis and emphysema was in a patient who had a small aneurism of the descending aorta directly behind the pulmonary veins, which was only 4 cm. in diameter and projected anteriorly from the aortic wall. The patient died suddenly from acute thrombosis of both pulmonary veins as a result of the encroaching aneurism.

The only acute disease of the respiratory path I have seen that is attended with dilatation of the right ventricle and auricle in which the left heart retains a normal size is gas poisoning. The inhalation of war

gas followed by acute lung œdema was frequently accompanied by acute dilatation of the right without involvement of the left side of the heart. This is satisfactorily explained by the extremely abundant thrombi in the pulmonary vessels.

Pulmonary Stasis.—Although, forty years ago, von Basch was wrong in his interpretation of the mechanism of lung rigidity from pulmonary stasis, he was right in conceiving lessened extensibility of the lung to be a direct and unfailing result of stasis in the pulmonary circulation. In recent years the study of lung rigidity from blood stasis has been resumed in the light of modern progress in the study of respiration and the measure of vital capacity of the lung has become a valuable method for procuring evidence both for and against the existence of pulmonary stasis. This is important for in some circulatory diseases the absence of blood stasis in the lungs is quite as important for a correct evaluation of circulatory hydraulics as its presence may be for a correct evaluation in other circulatory diseases. The absence of pulmonary stasis is of great significance in arterio-venous fistula and in congenital heart disease in which there is an open interventricular septum with stenosis of the pulmonary artery. In both these conditions there may be dilatation of both ventricles and of the right auricle and a strong systolic liver pulse without pulmonary stasis.

Also in chronic cardiovascular disease with nephritis attended with periodic breathing and the moisture of œdema in the air spaces of the lungs, there may be a perfectly normal volume flow of blood through the lung without pulmonary stasis. But in such a case the examiner might accept the moisture in the lung as evidence for pulmonary stasis when in reality the lung œdema is not the result of a failure in blood hydraulics, but merely a local accumulation of retained body fluid.

Signs of Pulmonary Stasis.—When there is stasis in the lung circulation as a result of cardiac decompensation the volume of blood within the pulmonary vessels is increased and is under increased pressure. These two (volume and pressure increase) alone are responsible for a diminution of the volume of the air spaces and also for lessened extensibility of the lung. With interstitial œdema and œdema of the visceral pleura the extensibility is further diminished, and when serum is poured out in the air spaces ventilation is still further diminished. It is not uncommon for the vital capacity of the lung to be reduced to 20 per cent. of the normal expected amount. With great reduction of the vital capacity air hunger follows and orthopnoea may ensue. The upright position is in most cases the position of choice merely because most persons have normally a vital capacity 200 to 500 c.c. greater in the upright than in the horizontal position, and therefore with great reduction in lung extensibility the upright position is either preferred or compulsory because the lessened capacity in stasis will not tolerate the subtraction from the vital capacity that attends the horizontal position. If under normal conditions a man has a vital capacity of 4000 c.c. seated, and 3700 c.c. lying, and then has the vital capacity reduced to 800 c.c. by pulmonary stasis he can ill afford to lose 300 c.c. by lying down, whereas the loss of 300 c.c. under normal conditions can be well afforded. When, however, lung stasis occurs in a person whose vital capacity in health is either undiminished or greater

in the horizontal position he will either be indifferent to his position or may prefer lying down to being seated. If the vital capacity is measured, lesser degrees of pulmonary stasis may be detected in cardiac patients who are capable of moderate exercise. An ambulatory patient who in health had 4000 c.c. may have only 2500 c.c. vital capacity, but with this respiratory ability he may be able to perform moderate exercise without air hunger.

Surface Body Temperature in Pulmonary Stasis.—If metabolism is unchanged when cardiac decompensation occurs the body temperature rises merely because the radiation of heat from the body surface is lessened; and as cardiac recovery takes place the blood temperature falls merely because radiation from the body surface increases with the resumption of a larger blood flow through the skin.

In former times the temperature of the body surface and terminal parts, fingers, nose and ears was routinely observed as evidence for failing circulation. In modern times this simple procedure is generally disregarded but it gives very dependable information on the cardiac output. When the body surface is warm there can be no failure of blood flow through the heart. The minute volume flow must be adequate or the body surface will not be cold. The converse of this statement is, however, not true. There may be an adequate volume flow through the heart, but on account of vasomotor disturbances there may be a marked diminution of blood flow to the skin. However, if with cardio-respiratory distress, as seen in some cases of cardiac enlargement with pulmonary oedema, the patient's body surface is warm, some other explanation for the pulmonary oedema than blood stasis must be sought.

The following observations illustrate this point: A man, aged forty years, who had always been in good health and did manual labor until a few days before entering the hospital was suddenly seized with air hunger. His greatest complaint was air hunger with Cheyne-Stokes respiration when awake, and sleep was much disturbed by slumber apnoea with waking hyperpnoea. There was marked oedema of the legs and trunk. The arterial pulse was celer in character with great pulse excursion and large pulse pressure. The arterial pressure was 204/56 with a rhythmic heart-rate of 80. There was choc en dome over the apex of the left ventricle which was in the sixth interspace 4 cm. outside the mid-clavicular line. The right ventricle was also enlarged but the right auricle was not demonstrably dilated. There were loud aortic systolic and diastolic murmurs. There was marked pulmonary oedema. Such signs seemed to indicate an insufficient cardiac output and also that the pulmonary oedema was the direct result of incompetence of the left ventricle. However, the body surface and terminal parts were warm which suggested that the retention of body fluid and pulmonary oedema were due to some other source than failure of blood hydraulics. The urine did not indicate a severe renal disease.

The patient was given 30 c.c. of tincture of digitalis in three days without the least improvement. Then citrate of caffeine in doses of 1 gm. daily was given for two days without effect. Novasurol was then given and followed by great diuresis. The oedema of the skin and lungs promptly disappeared and all respiratory discomfort ceased. The heart remained

unchanged but its volume perceptibly diminished. The arterial pressure now changed to 170/70 with unchanged rate. There was a drop of 34 mm. Hg in the maximum systolic and a rise of 14 mm. Hg. in the minimum diastolic pressure. The deformity of the aortic valves certainly was not altered by the diuresis. With the heightened output of water, œdema of the heart muscle could have ceased just as did the œdema elsewhere. With the consequent improvement in the muscle of the conus arteriosus of the left ventricle there was improved diastolic support for the aortic blood and the minimum diastolic pressure thus being elevated the compensatory rise in the systolic pressure was no longer required to provide an adequate output of the left ventricle.

Before the administration of novasurol, when the pressure was 204/56, the volume flow was in all probability the same as afterward when the pressure was 170/70. There was in this patient another bit of evidence to show that the pulmonary œdema was not due to blood stasis. When the lung œdema and respiratory distress were most severe the vital capacity was 2500 c.c. which was quite sufficient to provide respiratory comfort in a man whose expected amount was 3700 c.c. Had this man's pulmonary œdema been due to blood stasis his vital capacity would have been much less than 2500 c.c. However, the warmth of the body surface in the presence of cardiac enlargement and pulmonary œdema first suggested that a failure of blood hydraulics was not the cause of œdema of the lungs.

Similar experiences suggested that estimation of the proportion of heat loss from the lungs to the total heat loss in pulmonary stasis might throw some light on the problem of cardiac decompensation.

R. D. Leas of the Lakeside Hospital found that the percentage of heat loss in cardiac decompensation was greatly increased simply because radiation from the body surface was diminished. This reciprocal relation is quite important and gives a new significance to the old observation on the relation of a cool body surface to cardiac failure and also shows the significance of a warm body surface as evidence against cardiac decompensation in the presence of other evidence that might be readily accepted, as proof of failing cardiac output. A calorimeter was devised into which the patient breathes and enables the observer to measure the heat in the expired air. The moisture of the expired air is captured by calcium chloride so that the amount of heat lost from the lung in the vaporization of water can be measured. The oxygen consumption is then measured and thus provides a basis for estimating what must be the total heat loss from the body. With this method it has been found that 10 per cent. of the total heat loss in a normal person can be recovered from the expired air in the calorimeter. In heart decompensation with pulmonary œdema as much as 25 per cent. of the total heat given off is by way of the lungs. This result stands in contrast with observations on patients with Graves' disease whose oxygen consumption was increased 80 per cent. In these cases 10 per cent. or less of the total heat loss was by way of the lungs and there was only a 12 per cent. increase of lung heat loss, although the total oxygen consumption was increased 80 per cent. This confirms the clinical evidence for increased radiation from the body surface that is such a well known symptom of this disease.

The measurement of vital capacity of the lung is a very helpful device, not only for making the diagnosis of lung rigidity but also for estimating the degree of lung stasis. Diminished resonance and moisture in the air spaces as revealed by auscultation will in most instances give sufficient evidence for the existence of stasis in the pulmonary circulation, but there are occasionally instances of a high degree of pulmonary stasis without evidences of moisture in the air spaces. The loss of lung extensibility as shown by the vital capacity reduction gives us a very simple method by which we can gain some conception of the degree of hydraulic failure of blood flow from the right to the left ventricle. When the left heart fails to maintain its output and the right heart persists in its work, rigidity of the lung is ineluctable, although foamy expectoration tinged with blood may be wanting and auscultation may reveal no rales. It should also be remembered that when a genuine hydraulic failure of the left heart occurs the body surface is cool and also that when the heart's chambers are enlarged in the presence of pulmonary œdema, and the body surface is warm, there cannot be a failure in the output of the left ventricle.

Hydraulics of Blood Flow and Massing of the Blood in Cardiac Diseases.—Anyone who has much experience in handling cases of failing circulatory function must be greatly perplexed if he attempts to trace a dependent relation between varying volume flow through the heart, the massing of blood in the pulmonary and systemic veins, the relations between incompetent output of the heart and the location of œdema and serous transudates. A patient may have enlargement of the heart chambers, pulmonary œdema, general anasarca and great respiratory distress, and by different kinds of treatment be relieved of the retained body fluid and blood stasis in varying locations with a return to respiratory comfort, but afterward we are often in doubt as to the exactness of our views about the pathological physiology. We may trace the improvement in cardio-respiratory function to the use of antisymphilitic treatment, digitalis, some theobromine preparation or novasurol, but if we try to trace the improvement of symptoms to enlargement of the heart's output, we are often unable to prove that there has been any change in the volume flow of blood. The cardio-respiratory function is much improved but we are unable to prove that the output of the heart has been increased. Thus far there is no dependable method devised by which we can accurately estimate the heart's output. An accurate method that can be used to determine the minute volume flow of blood through the heart in varying cardio-respiratory efficiency will contribute more toward improving our clinical criticism than any single contribution to the subject that has thus far been made. In spite of our competence to estimate the size of the heart's chambers, the pulse-pressure, pulmonary œdema, stasis in the large veins, volume of the liver, and renal function we are often unable to translate this collected data into an accurate interpretation of blood hydraulics. There seems to be in the course of cardiac and cardiovascular diseases some alteration in the body cells, or in the blood which alters the normal lymph flow quite independently of blood-pressure and blood flow through the heart and large vessels. The mobility of fluids from the bloodvessels to the extravascular spaces and from the extra-

vascular spaces to the bloodvessels, the holding of water so that it is not properly released to the renal filter and also the abnormal fixing of water to the body cells are problems that require solution before we can satisfactorily interpret the pathological physiology of the circulation. It seems that before these can be solved the way must be cleared of the confronting problem of volume flow. As matters now stand this perplexing question complicates all the problems of respiration, blood massing, lymph flow, œdema and renal output. When each one of these propositions can be disentangled from the basic problem of heart output a long stride will have been made toward the evaluation of many symptoms in heart disease that is now denied us.

Serous Accumulations.—In what apparently seem to be cases of pure cardiac disease and also in cardiovascular disease there is not a direct sequential relation between lessened volume flow of blood and the accumulation of serous effusions. This is particularly true of cardiovascular disease which has existed for a long time and also in old cardiovalvular disease. In chronic myocardial disease that has produced no symptoms until cardiectasis suddenly supervenes, or in acute cardiectasis as a result of pneumonia, or in acute cardiectasis in mitral disease, the resulting stasis in the pulmonary circulation with pulmonary œdema, dilated veins and engorged swollen liver follow in sequential relation. But this sequence of events does not happen in the chronic cases. In the old cases pulmonary œdema may be conspicuously present and the other evidences of stasis be wanting, or there may be hydrothorax and no pulmonary œdema, and no evidence of engorged veins and swollen liver. It is particularly in chronic mitral stenosis that we see great ascitic accumulations without the expected pulmonary œdema or even stasis in the pulmonary veins that we might expect. This change in the sequence and order of events in the chronic cases cannot always be explained by incompetent kidneys nor by lessened volume blood flow through the kidneys. The accumulation of serous transudates apparently is due to some regional disturbance in the factors that determine the normal relation between endovascular and extravascular fluid. The transudate is not traceable to failing hydraulics in blood flow but to some biological change in the tissues. Whether the cause is altered permeability of the cell membrane or a clinical change in the cellular content is not known. Clinical experience, however, teaches us that in chronic cases regional dropsies cannot always be explained by regional hydraulic failure of blood flow.

Neither hydremic plethora nor hemic plethora is adequate to explain this very common occurrence. The explanation must await further progress in our knowledge of the biology of the cell. If one conceives of heart and vascular diseases as revealing a long course of symptoms and pathological complications that must be traced to graded failures in blood hydraulics he will be disappointed, for such simplicity does not exist. The chronic heart and valvular diseases become biological as well as physical problems. If we had to deal only with blood hydraulics our therapeutic problems would soon be answered in a positive or negative sense. The following example opens the way for speculation on all the factors above mentioned. A patient with chronic cardiovascular disease has enlarged heart chambers, a moderate amount of moisture in the air

spaces of the lungs, a right-sided hydrothorax of about 1 litre, œdema of the trunk and legs and air hunger with periodic breathing. Cardiac stimulants and diuretics fail to give relief. After these measures have failed 1000 c.c. of serum are aspirated from the pleural cavity. Within a half day the patient is enjoying respiratory comfort and all œdema has disappeared. Should one hold that the removal of a litre of serum from the thorax has greatly improved the mass movement of blood and in this way relieved dropsy and air hunger, I believe him to be wrong. The mass movement of blood through the heart is unchanged by the thoracentesis. The explanation for the relief lies nearer the life of the body cells than a change in volume flow or in the relation between the vascular reservoir and the amount of endovascular blood. In the clinical study of heart disease we soon come to an end of our knowledge if we seek to interpret all the events on the basis of blood hydraulics. The clinician finds that the physics of blood flow do not support him very far in the interpretation of cardiac symptomatology or guide him very far in the therapy of chronic cardiac and vascular diseases.

Air Hunger.—This is purely a subjective experience and when caused by a disturbance in the physiology of respiration is always associated with hyperpnœa, dyspnœa, tachypnœa or periodic breathing. Many patients appeal for relief from a nervous experience which they describe as “shortness of breath.” The subjective experience is described as the feeling of an unsatisfactory inspiration. They say they cannot get a satisfactorily deep breath and are constantly trying to distend their lungs beyond their normal capacity for extension. They do not superventilate but merely make long deliberate efforts to extend the lungs beyond their normal capacity with the hope of getting rid of a nervous discomfort located in the epigastrium. These patients get relief by yawning or gaping, which satisfies the sensation of air hunger. They can be satisfied if it is shown that genuine air hunger is always attended with an increased rate or volume of respiration and that one who has genuine air hunger cannot take time to yawn. They promptly recover if they are taught to exclude respiration from their field of consciousness. A much rarer experience is to find a hysterical patient who does actually superventilate the blood in response to a pure psychosis. These patients develop a genuine tetany as a result of alkalosis. The physician is usually called on account of the tetanic contractures of the forearm and hand muscles. The fact that tetany accompanies rapid respiration without any evidences of cardio-respiratory disease is sufficient to indicate superventilation as the cause of the tetany. If the patient cannot be persuaded to cease superventilating a hypodermic injection of morphine or some sedative will allay the nervous excitement which causes the trouble.

Tachypnœa without superventilation may be a symptom of a neurosis and demands the same kind of treatment as the cases just described or it may have its origin in a disturbance of the rate of automatic respiration that lies quite outside the field of consciousness. The instances of this curious symptom that have come under my observation were cases with either syphilitic or tuberculous mediastinitis. The only physiological experiment that throws any light on this symptom is found in the results obtained by stimulation of the pulmonary branch of the vagus. In dogs

the result is an arrest or slowing of the heart beat attended with rapid small respiratory excursions that are taken off the height of the inspiratory phase of lung expansion. This is exactly what happens in patients with mediastinitis.

Case.—A man, aged fifty years, who had been one week in the hospital on account of myocardial decompensation associated with syphilitic aortitis was seized with frequent tachypnœa and bradycardia which lasted for several hours unless relieved by morphine. These attacks occurred for several nights and were described by the interne as attacks of asthma. An attack began as the pulse was being palpated. The pulse-rate, which was 80 per minute, suddenly dropped to 40 per minute, and after two or three of the slowed cardiac cycles the respirations which had been 20 per minute suddenly rose to 60 per minute. The respiratory excursions were very shallow and were taken off the height of a moderately large inspiratory phase of the lung. The patient was anxious and much perturbed; he sat upright resting on his elbows and exhibited an apparent discomfort that strongly suggested asthma but for the very rapid thoracic excursions with unimpeded entrance and exit of air from the lungs. Atropine hypodermically stopped both the bradycardia and tachypnœa in ten minutes. The patient was protected against a return of his attacks by receiving 1 mg. of atropine sulphate twice daily by mouth. Vigorous antisymphilitic treatment cured him of the irritative lesion in the mediastinum. This patient on being asked to describe his respiratory distress said it was unlike the experience of air hunger that follows physical exercise but that he had a feeling of constriction across the upper thorax which constrained him to breathe very rapidly. This he did without superventilating his blood. During the attack there was no change in the size of the heart or volume of the veins and there were no abnormal sounds heard over the lung, nor was there any enlargement of the lungs.

Slumber Apnœa and Waking Hyperpnœa.—Patients who have this experience usually appeal to their physician for relief from "nocturnal asthma." On inquiry, however, it will be learned that the patient awakens out of sleep with intense air hunger that compels him to sit up and breathe very rapidly and deeply for a few minutes. These attacks come so frequently that the patient fears to go to sleep and then after great exhaustion he can sleep without interruption. In former years this symptom caused much perplexity and was suspected of being caused by some abnormal afferent impulse in the depressor nerve which supplies some end branches to the root of the aorta. This origin was suspected because the symptom was usually observed in patients who had arteriosclerosis with evidences of involvement of the root of the aorta. No change in the size, rate or rhythm of the heart was found. The pulse was unaltered in character and there was no evidence of resistance to the entrance or exit of air from the lungs. The apnœa that preceded the hyperpnœa on waking, however, had been overlooked and gave rise to the fanciful explanation advanced by Huchard thirty-five years ago.

It is surprising to see how this disturbance in automatic respiration will disturb a man who has no other subjective symptom of cardiovascular disease. The first patient in whom this train of events was recognized, twenty years ago, complained of what he believed to be a nervous dis-

order and to overcome this he went hunting during the day, walking over ploughed fields covered with snow, climbing fences and carrying a gun. From all this exercise he experienced no sense of fatigue and yet he had marked arteriosclerosis with hypertension and a hypertrophied left ventricle. In spite of his ability to exercise he carried a potential apnoea due to impaired arterialization of his brain which with the added hypoesthesia to his respiratory centre that comes with sleep he had apnoea that would last nearly a minute. A curious feature of this symptom lies in the fact that it comes in light and not in deep slumber when *a priori* the symptom would be expected to occur.

The same symptom occurs in meningo-angiitis syphilitica of the brain, a disease in which defective vascularization of the brain is responsible for most of the symptoms. One patient of this kind employed a nurse for the sole purpose of watching at night and wakening him should he cease breathing as he went to sleep, for by this he was spared the long period of apnoea which was followed by waking with great air hunger. After repeated efforts to go to sleep and continue to breathe, toward morning, when he was quite exhausted, he would lapse into a deep slumber and continue his automatic breathing.

Few patients with cardiovascular disease run their whole course without developing slumber apnoea at some period. It may be the first subjective sign of disease or it may come on after myocardial incompetence begins to make itself felt, or it may not come until after the patient is bedridden with dropsy and asystole. The chemistry of the blood and the respired air does not explain the phenomenon. Some alteration in the function of the respiratory centre seems to be responsible and inferentially we have reason to believe that impairment of the circulation is the cause at least in some of the cases, but ischemia or anoxemia of the cells does not satisfactorily explain all the cases.

Hypothyroidism.—Another condition in which slumber apnoea and waking hyperpnœa point the way to recognition of the underlying pathology is hypothyroidism. A patient was in the hospital for several weeks on account of general œdema which could not be explained by disease of the heart or vascular system or by incompetence of the kidney. On a salt-free diet she was relieved of her retention of body fluid and left the hospital. Later she came to the dispensary with a return of her œdema, but she complained of waking hyperpnœa which aroused the suspicion of hypothyroidism on the theory that her lowered oxygen metabolism was still further lowered in sleep and with the added hypoesthesia of the respiratory centre that comes with sleep the potential apnoea of her waking hours became effective in slumber. The patient was readmitted to the hospital and her basal metabolism found to be 25 per cent. below the expected amount. She was then allowed a liberal mixed diet and thyroidine was given at the same time. All the retained body fluid was eliminated and the slumber apnoea with waking hyperpnœa promptly ceased. Further observations on this patient proved that her retention of body fluid and slumber apnoea were not the only signs of myxœdema, for the patient's mental and physical vigor was greatly improved by thyroid feeding.

CHAPTER XIII

DISEASES OF THE PERICARDIUM

BY ALEXANDER McPHEDRAN, M.D., LL.D.

ACUTE PERICARDITIS

Introduction.—The pericardium is a fibrous sac with a serous lining. Its outer fibrous layer, dense and resistant, forms a tubular prolongation along the large bloodvessels and becomes fused with their external coat and the cervical fascia. The inferior vena cava passes through the right lower angle of the pericardium to reach the heart. The serous membrane lines the sac and is reflected over the surface of the heart, forming the epicardium. It forms a common tubular sheath for the first portion of the aorta and pulmonary artery. It is also reflected on the superior vena cava and pulmonary veins. The pericardium is firmly attached below to the central tendinous part of the diaphragm; anteriorly, loosely to the sternum and costal cartilages; posteriorly, to the roots of the lungs and other mediastinal structures and on each side it is attached to the pleuræ which extend to a varying degree over the anterior and posterior areas, in places coming into contact with each other. The internal surface of the sac is glistening and moistened by a serous secretion, thus affording free play for the movements of the heart with the least possible friction.

The pericardium gives a measure of support to the heart in its movements and many changes in volume. Owing to its firm attachments above and below, and the traction of the lungs on each side acting as ligaments, it maintains the thoracic structures in their relative positions.

Although it is clinically convenient to consider diseases of the pericardium, endocardium and myocardium separately, there is much to be said for the opinion of the late Sir J. Mackenzie that it would be better to study them under the one term of *carditis*, as the heart is a single structure. The division was introduced in the early history of medicine before it was known that no infection is confined to one structure alone. While pericarditis may occur without endocarditis, neither of these occur without infection of the myocardium as well. It was only with the advance in pathology that we became cognizant of this fact although it was long known that all three were frequently simultaneously infected; also that in disease in the endocardium or pericardium, the myocardium is always infected, so that a pathological examination is not complete without examination of the muscular structures.

Etiology.—*Pericarditis* is said to be rarely a primary disease except by infection through a penetrating external wound or one caused by a foreign body lodged in the œsophagus. But pericarditis so often develops insidiously, and is only discovered in a routine examination, especially in

renal cases, that its occurrence as a primary infection must be greater than has been realized. Its insidious development may be due to its relatively scant arterial supply. It is said to be rare in children under five years of age and in elderly persons; but in both of these groups, diagnosis is especially difficult, so that many cases may escape detection. It occurs oftenest in males, doubtless because of their life of greater exposure and strain at the age of greater prevalence of infections, rheumatic and septic. Signs of the disease have been found in the fetus and the newborn have been infected through the umbilical cord. Infection of the pericardium may take place through the blood, by direct extension from disease of an adjacent part or through the lymphatics.

Rheumatic infection, mild as well as severe, is by far the most frequent cause of pericarditis. This was first pointed out by Pitcairn in 1788. There is a growing conviction that the rheumatic infection first involves the throat, especially the tonsils, enters the blood stream, and infects the joints, the heart and other parts, especially the serous membranes. It is probable that the various seats of infection are usually primary and not dependent on each other. The joints have been long regarded as the most frequently infected, but this view may be doubted, owing to the fact that in most, if not all, cases of rheumatic fever, the heart is enlarged in some degree even without other signs of disease, the damage not being sufficient to cause murmurs or other signs.

Pericarditis usually becomes evident about the second week of an attack of rheumatic fever. The early symptoms are easily overlooked especially in children. Gibson found that it is not nearly so dependent on previous attacks as is endocarditis; it is liable to occur in cases of chronic endocarditis in which the heart is enlarged. In such cases it is usually confined to the membrane over the aortic ring, and probably caused by infection passing through from the diseased valves. Of the frequency of pericarditis, opinions vary widely so that statistics are of little value. The chief reason for this lies in the fact, that owing to the difficulties of diagnosis, many cases escape detection. In 150 fatal cases of rheumatism in children Poynton found that 113 showed signs of pericarditis at necropsy. Vigilance is the price to be paid for better diagnostic results.

Chorea is occasionally associated with pericarditis; more frequently still with endopericarditis. The cardiac affection may precede the choreic movements. There was pericarditis in 19 of 73 cases collected by Osler; in only 8 of these was there a history of arthritis. Pericarditis has also been met with in *erythema nodosum*. The *gonococcus* is an occasional cause of pericarditis, the organism being present in the exudate. It is a more frequent cause of endocarditis.

In *pneumonia*, the occurrence of pericarditis is usually met with in severe cases affecting two or more lobes, especially the lower. In many such cases there is empyema and to it the pericardial infection may be directly due. Preble found pericarditis in 92 per cent. of 79 cases. In such cases the signs may be so masked by the pulmonary symptoms, that they are not only easily overlooked but may be impossible of discovery. The pericarditis is often purulent, the pneumococcus being nearly always the infecting organism. In alcoholics it may occur when there is only a

distant small area of pneumonia. *Pneumococcus pericarditis* may occur without pneumonia, as in nephritis. Other parts may be infected, as the joints and meninges.

Septic infections probably cause pericarditis more frequently than the records indicate. In a recent case, the patient, suffering from septic pneumonia, coughed in the face of the physician, who had a sore throat the following day. The pericardium must have been infected shortly after as there was rapid effusion and great distress three or four days later. The pericardium was promptly opened and 600 cc. of pus evacuated in which streptococci were found. There was friction at both pleural bases at the same time but this gradually disappeared. The drainage was effective but as a result of increasing myocarditis death occurred a few days later. Such cases may arise from local septic infections of any part, as the abdomen, from furuncles with lymphangitis, erysipelas, mastoid abscess, meningitis, or septic infections of bones and joints.

Scarlet fever may be a direct or indirect cause of pericarditis. Like nephritis it occurs about the second or third week. Arthritis is not uncommon and is possibly the source of the pericardial infection, but more probably both result from a common cause.

Tuberculosis is a cause of pericarditis but just how frequently it is not possible to say, as in many instances no complaint is made to indicate local trouble in relation to the heart; and of many deaths so few come to necropsy. The pericardium is always infected in general miliary tuberculosis but without local symptoms to indicate this or, it may be, any other part. If the general disease is not rapidly fatal, there may be a dry, slowly progressive inflammation ending in general pericardial adhesions.

In others tuberculous pericarditis is often a symptomless infection with effusion, often very large and with signs that mask all evidences of the disease in the pleura or mediastinal glands, usually the source of the infection.

In *renal disease*, pericarditis is usually so quiescent that in many cases no suspicion is aroused. It is of frequent occurrence, probably only less so than in rheumatic fever. The only complaint may be of some languor and of becoming easily fatigued. Loss of color with some anemia is frequent. A general examination may reveal a loud persistent pericardial friction. In the old, the renal lesion is interstitial; in the young, parenchymatous.

In the other acute infectious diseases, pericarditis is very rare, mumps, measles, whooping-cough, malaria, diphtheria and smallpox; purulent in the last. In typhoid fever, McCrae found 3 in 1500 records. In influenza, the cause of so many various local infections, the pericardium is only rarely directly infected, but as a secondary infection to empyema and pneumonia, it has been very frequent in later epidemics. It is infrequent in cerebrospinal fever but has been found at necropsy.

Pathology.—If the infection comes through the blood the inflammation usually appears first in the epicardium about the branches of the coronary arteries; if by extension or through lymphatics to the pericardium, except when from the aortic valves, it infects the visceral layer and the base of the heart, and later, to a less extent, the corresponding parietal membrane.

Its surface becomes reddish due to a visible vascular network. There is some serous and leukocytic exudate which causes swelling of the endothelium and loss of the normal glistening appearance. If the process is transient, the exudate is arrested, the serum and leukocytes are absorbed and the membrane returns to its normal condition. Usually, however, the pathological process increases, the surface becomes velvety and thickened, endothelium separates, serum exudes and minute hemorrhages occur. New and larger arterioles appear with increasing transudation and diapedesis; the effusion increases and fibrinous flakes with many leukocytes are cast off. The fibrinous layers thicken and can be rubbed off as gelatinous masses or form into ridges by the movements of the heart. In many acute cases, masses of organisms are present in the fibrinous exudate. Later sero-fibrinous fluid, often bloodstained, may become purulent accumulations of indefinite quantity. The exudate varies from a few cubic centimeters to 300 or 400 cc., not usually much greater, in acute sero-fibrinous cases. In slowly progressive cases, 2 liters or more may be found, especially in tuberculous cases. In a boy, aged twelve years, under the writer's care, 1400 cc. of sero-sanguinolent fluid were removed in the third aspiration. On the other hand the exudate may remain fibrinous.

Large effusions are a serious menace to the action of the heart by compressing the auricles and impeding the entry of the blood into the ventricles. They may compress the lungs to such a degree as to cause collapse, especially the left. In purulent cases ulceration may take place toward the surface of the body or in other directions. Hemorrhage may occur from rupture of the new vessels in the fibrinous exudate. It is most frequent in tuberculous cases. It is met with also in the aged and alcoholics, and with scurvy, cancer and cachexia.

In most sero-fibrinous cases, even with marked effusion, recover follows without drainage, especially in those due to rheumatic fever. Absorption follows granular and fatty degeneration of the fibrinous membrane, the only exception being the organization of bands by the fibroblasts carried by new bloodvessels into fibrinous exudate. Chronic inflammation may extend to surrounding tissue and give rise to chronic mediastinitis. Myocarditis, in the outer part of the heart at least, doubtless occurs in all cases simultaneously with the pericarditis.

Symptoms.—The most striking characteristic of pericarditis is the absence in so many cases of definite symptoms. Even acute cases may be obscured by grave diseases in the chest, especially in severe pneumonia.

In contrast to dry pleurisy, pericarditis is regarded by some as a painless malady. Definite pain is an evidence of associated myocarditis (Sir J. Mackenzie). Usually there is a dull feeling of distress and oppression rather than pain in the precordium, often increased by movement, deep inspiration, cough and external pressure. The expression is somewhat anxious even in mild cases. The attitude is often significant—sitting a little forward and to the left, and quite still, probably an indication of infection of the myocardium rather than of the pericardium. The respiratory and general movements are restrained. If the diaphragm is involved, it is fixed and there may be the most extreme pain such as

occurs in cases of basal pleurisy in which the inflammation extends into the diaphragm in which even the largest dose of morphine gives no relief. As the œsophagus lies in contact with the pericardium the passage of food and liquid may be painful. Besides tenderness in the precordium, especially in the intercostal space, a tender point may be found over the phrenic nerve above the clavicle between the two chief insertions of the sternomastoid muscle, and a second point between the left costal margin and the xiphoid cartilage.

Angina pectoris, as pointed out by Stokes, is met with in some cases. The pain begins in the precordium and extends to the left, followed by numbness, with or without pain in the left arm, dyspnœa, disturbed action of the heart, great anxiety, threatened syncope, pallor, and coldness of the limbs. The outlook is grave, especially after the meridian of life. The temperature is usually elevated moderately and the pulse rapid but otherwise unaltered. The anginal attack may be due to inflammation of the pericardium overlapping the aorta, and its extension to the sensitive adventitia of that vessel (Allbutt).

Physical Signs.—There is usually a slight appearance of fulness in the precordium, owing to paresis of the intercostal muscles in adults; in children there may be a general symmetrical fulness due to the elasticity of the wall of the chest. The immobility that may result from the effusion adds to the appearance of fulness. The fulness may be increased by dilatation of the heart, a frequent, if not constant incident in cases due to rheumatic fever. In this early period, *pericardial friction*, so significant, is usually heard and is easily recognized. It is not radiated and lessens with an increase of the effusion. Its intensity is no indication of the degree of inflammation; it is frequently loudest in cases due to nephritis. It may cross with endocardial murmurs and be difficult to differentiate from them. Laënnec discovered the sound, but it was not properly interpreted until described by his assistant, Collin, in 1824. It occurs in both systole and diastole as a to-and-fro sound or vibration. It is usually heard first in the second or third intercostal spaces, less often along the left border of the heart, over the lower end of the sternum, or at the apex of the heart; later it may become general over the whole surface of the heart, but more often extends gradually toward the apex, in the meantime disappearing at the base.

The character of the sound varies; it may be soft like the rubbing of tissue paper, or harsh like the creaking of new leather, or like the sound of scraping or scratching of rough paper, especially in chronic cases. It is superficial and may even seem to pass between the thoracic wall and the ear of the observer. It may be increased by firm pressure with the stethoscope; Gibson pointed out that, if the pressure is too heavy, it may be weakened or even arrested, especially if the heart is weak. It is usually increased when the erect position is assumed and lessened in the recumbent posture. Exciting the heart's action may also increase it.

The duration of the friction sound is variable, in some cases it lasts but a few hours, and in others throughout the greater part of the course of the disease. Its disappearance may be due to absorption of the exudate, adhesion of the opposing surfaces, or increase of the exudate, plastic or

serous. If the heart is held against the wall of the chest by adhesions or other cause, the friction sounds may persist even after copious effusion. When the exudate is absorbed the roughened pericardial surfaces again coming into contact may cause a recurrence of the friction.

Non-inflammatory dryness or loss of smoothness of the serous surface, ecchymoses, and "milk spots," may cause a similar friction sound, especially if cardiac hypertrophy increases the energy of the heart's contraction, as was shown by Stokes and Graves.

The *respiratory movements* have a variable influence on the area and intensity of the sound; in some cases it is loudest in expiration, in others in inspiration. Its area is often increased below during inspiration and, less often, above in expiration (Sibson). It is almost always limited to the precordial area. There are some exceptions to this, however, especially during the decline of effusion; Sibson, in 1 case, found the friction sound audible over the greater part of the front of the chest, especially in the lower part. Vibration from the friction may be felt by the hand placed on the precordium, as a peculiar vibrating or scratching sensation especially if the sound is loud and rough. It gives the impression of being quite superficial. It lacks the characteristic vibratory character of the thrill of mitral stenosis.

The effect of *effusion* depends on its rapidity, quantity, and the integrity of the heart. Rapid effusion, even moderate, increases precordial distress and impedes the filling of the auricles. Cohnheim and, later, Starling showed by experiments that injection of 20 cc. of water into the pericardial cavity causes signs of increased pressure on the auricle, and the addition of 10 cc. will obstruct their filling, as shown by a rise in venous pressure and a fall in arterial pressure, the result being distention of the jugular vein and a small weak pulse from lessened supply of blood to the ventricles. Not until then is the pulse altered and dyspnoea present. If part of the injected fluid is aspirated the normal venous and arterial pressures are restored. In the pathological condition, however, much will depend on the state of the pericardium and the integrity of the myocardium.

Large effusions, if slowly formed, do not cause such marked signs as the pericardium is slowly dilated and has lost much of its tone from the inflammatory changes. Consequently it is rarely that the heart is seriously embarrassed by slowly formed and even very large effusions, unless the heart itself is gravely damaged.

With increasing intrapericardial pressure and lessening efficiency of the heart, the pulse becomes small and weak and increases in rapidity, more so than the respiration. Expiratory filling and inspiratory emptying of the jugular vein, and corresponding changes in the pulse—the *pulsus paradoxus*—result from pressure on the vena cava by the distended pericardium, by mediastinitis or other cause. In marked cases there may be considerable anoxemia. If the aorta is compressed there will be a small pulse in inspiration, due to the increased intrathoracic pressure, and a large one in expiration. It must be distinguished from the respiratory irregularities met with in children and sometimes in women and young adults. Recently a small boy was brought to the writer on account of

such irregularity for which he had been kept in bed for a year. With complete freedom of activity, the irregularity disappeared in a few weeks.

Percussion gives considerable aid. In small effusions with no adhesions, there may be flatness in the right lower part, converting the acute cardio-hepatic angle into an obtuse one. As the effusion increases the area of dulness extends in all directions; if large to the right of the sternum; on the left to the axillary line with a curve inward in the upper part (Sibson's notch); upward to the second rib or even above it; and downward into the costo-xiphoid angle, the whole area forming an unchanging pear-shaped area with the base downward. The heart impulse is usually pushed upward to the fourth space well inside the line of dulness and is usually feeble. If the effusion is very large, there may be a dull patch below the left scapula, often mistakenly regarded as due to pneumonia or pleural effusion. It may disappear in the prone position. It should be noted that a greatly dilated heart from myocarditis may produce an almost identical result. Its impulse is weak and not from the apex but from the anterior surface of the heart and therefore well within the left margin of dulness; it is usually more marked on leaning forward or in the prone position. Change of position may alter its position, not so with fluid. The dull area may vary hourly or daily and should therefore be frequently examined.

Auscultation is of much importance; it often gives the first clue by the *to-and-fro* friction sound, heard usually in the second and third spaces over the area in which it is produced. It is superficial, and with rare exceptions, definitely circumscribed and not radiated. It does not indicate the degree of inflammation. In rare cases the area over which it is audible may be wide, and it may be heard behind if the left lung collapses and the heart is large. This wide-spread area may be due to friction from inflammation extending over the whole surface of the heart. The friction sound may be increased or decreased by pressure of the stethoscope; it may alter from hour to hour, with change of position, with respiratory movements of the chest, and be weakened or disappear in the dorsal position. Inflammation of the pleura overlapping the heart may cause a friction sound synchronous with the heart beat; unless adherent, it will be altered in respiration. Holding the breath after a deep inspiration may aid in deciding its cause.

Before the rub is audible, a gallop rhythm or trembling of the heart may be heard, due presumably to a sticky action between the coats of the auricle and ventricle (Allbutt). With increase of the effusion, the friction sounds disappear and the heart sounds grow weaker, unless adhesions hold the fluid back, in which case the roentgen-ray may show the signs of such condition.

The further history of the effusion varies with its cause and nature. In rheumatic cases, with arrest of the disease, absorption usually progresses rapidly; as the area of dulness lessens, the friction rub may reappear, altered and less regular; the heart impulse and sounds become more distinct; the temperature falls and the pulse becomes less rapid; and the general condition improves. If there has been serious myocarditis, improvement will be slower and the ultimate outlook will depend on the

degree of damage to the heart. If the cause is tuberculous, the effusion often continues to increase, largely depending on the general condition. A serous effusion may become *purulent*; if so, the effusion increases and it may be large. The general conditions will indicate a mixed infection. But purulent effusions are usually such from the beginning.

Diagnosis.—The existence of pericarditis is very frequently overlooked. Its course in many cases is so insidious and the signs so indefinite that its existence is not suspected and a careful examination is therefore not made. Another reason is because it is so often associated with other diseases, especially pneumonia, which overshadow its symptoms and frequently so obscure it as to make a diagnosis impossible, or, at most, only probable. Such symptoms as pain in the precordium, the tender points along the course of the phrenic nerve, the quickened respiration, anxious countenance, and venous stasis may indicate its occurrence, but, then most of these symptoms may be present also in pneumonia, in diaphragmatic pleurisy, in endocarditis, and especially in myocarditis.

The diagnosis offers no difficulty if the *friction sound* is distinct and characteristic. It is of sudden onset, usually audible over a small area, and vibration may be felt by the hand. The existence of endocardial murmurs may cause difficulty, especially if *loud*. The effect of pressure by the stethoscope, the time rhythm, and the effect of respiration are usually sufficient indications of the true nature of the condition.

In mild subacute attacks of pericarditis, especially in children, the onset is so insidious that the disease may exist for several days, and the heart may have suffered serious damage before the child is considered to be seriously ill, and even then it is only after a careful examination, in which the signs of pericarditis are sought for, that the actual condition is recognized.

In *dilatation* of the heart there may be all the signs of effusion, even the dull area below the scapula, and the impulse of the heart may be near its normal place. Enlargement of the liver is usual and significant. In pleural exudate, if considerable, the heart is displaced to the right. Error in diagnosis has led the most experienced observers to aspirate for the removal of a pleural exudate that did not exist; the right ventricle has been punctured, but fortunately without any injurious effect. Even paracentesis does not necessarily determine the presence or absence of fluid in the pericardium; the heart may lie in front of the fluid and prevent access to it; as may also great thickness of a plastic exudate; and plugging of the aspirating needle may mislead.

By the use of the *roentgen-ray screen* a momentary clear space between the heart and diaphragm may be seen for a second or two during a very deep inspiration in most cases. The patient should bend well to the left side in order that the left lung may push the outer pericardium from apex to the vena cava, forward against the anterior wall. In large pericardial effusions the central part of the diaphragm is depressed to its lowest limit and immobile, so that in the deepest inspiration no clear space could occur. In such cases also there is narrowing of the subcostal angle with each inspiration, due to the activity of the diaphragm.

Effusion into the left pleura may simulate pericardial effusion, and *vice versa*, especially if the pleural fluid is encysted and in the neighborhood of the pericardium. The shape of the dull area, the condition of the lung, the tone of the heart sounds and especially displacement of the heart to the right, the fact that pericarditis is nearly always insidious in onset and develops silently, should suffice to differentiate the two conditions even if the pericarditis follows the pleural disease. The coexistence of both pleural and pericardial effusions may be more perplexing, but the signs peculiar to each are usually sufficient, as a rule, to guide to a correct diagnosis. Puncture may solve the difficulty; if not the roentgen-ray study usually does so.

Affections causing induration of the lung overlapping the heart, tumors in the mediastinum, and aneurisms of the aorta, all may increase the area of precordial dulness, but are distinguished from pericardial effusion by the form of the dull area and other symptoms and signs of these conditions.

In the determination of the nature of the *effusion*, the physical signs afford no assistance; the general phenomena, such as the course of the temperature, the general condition of the patient, the coexisting affections, and, above all, the cause of the disease, may furnish indications sufficient to decide whether the exudate is serofibrinous, purulent, or hemorrhagic. But in many cases the nature of the exudate can only be determined by withdrawing some of the fluid, as the character of the infection on which the pericarditis depends does not necessarily determine the nature of the exudate. Thus, in tuberculous cases the exudate may be serous or hemorrhagic; in rheumatic cases it is usually serous but may be purulent; and in septic cases, although usually purulent it may be serous.

Chronic pericarditis is ordinarily the sequence of an acute pericarditis in which recovery has been arrested in the course of the absorption of the exudate. But in some cases the affection develops so imperceptibly as to merit the appellation when first discovered, particularly in the aged, in chronic nephritis, in the tuberculous, in alcoholics and in the debilitated. When chronic pericarditis succeeds the acute form the effusion may be stationary or gradually diminish, but may increase from time to time with a return of acute symptoms, and there may be signs of increasing myocardial degeneration, as indicated by the circulation becoming less and less efficient. In some cases the exudate is gradually absorbed, and the pericardium may become adherent over the whole surface of the heart.

Prognosis.—Pericarditis due to rheumatic fever in an otherwise healthy individual may, and usually does, disappear after two or three weeks without leaving any clinical traces of its occurrence. However, even in such persons, there has been at least superficial infection of the myocardium from which some degenerative changes of muscle tissue must result. There is probably frequently, if not always, some endocarditis also, even without physical signs, leaving greater liability to infection in subsequent rheumatic attacks should such occur. Pulmonary, pleural, renal or other complications may seriously alter the outlook. Even without such complications the disease must be considered as serious, not so much in itself, as the pericardium is not a vital structure, but in the fre-

quent associated conditions, especially myocarditis; which is, in the last analysis, the cause of a fatal ending in the majority of cases. In some instances in the adherent pericardium there is a persistent proliferation of dense fibrous tissue which gradually embarrasses the heart. This process may extend to the mediastinum and cause dense adhesions to all the neighboring structures.

In the chronic renal cases the prospect is grave, owing rather to the renal than the pericardial lesion. In children the chief danger arises from the heart itself, especially its muscular tissue. In them the disease often runs an acute course and necropsy reveals complete disorganization of the muscular structures.

Treatment.—In mild cases of pericarditis the ordinary treatment of rheumatic fever suffices. The effusion, usually moderate, does not often materially affect the heart's function, and is generally duly absorbed and therefore calls for no special treatment.

For the relief of pain and oppression, cold is probably the most effective means. Its intermittent application may be better than continuous, as the latter may cause dilatation of the vessels after a short time and recurrence of discomfort. The affect of alternate heat and cold on the bloodvessels is well illustrated by the shrivelled state of a washerwoman's hands in winter, caused by the alternate washing in the hot water and exposure to the cold air while hanging out the clothes. It is also to be borne in mind that cold materially raises the blood-pressure and may cause too much strain on the heart if its muscle structure is seriously affected. Leeches applied to the precordium relieves pain and are preferable if the heart shows signs of weakness. A few small blisters, or repeated hot applications may be equally effective. Sedatives should be given when required.

In rheumatic fever, the effusion is usually moderate and readily absorbed; a blister may hasten this. If delayed the pulse may become weak, with dyspnoea and faintness. Aspiration is generally followed by relief. Not rarely, however, these symptoms are due, chiefly, if not wholly, to dilatation of the heart. A moderate effusion, if present, in a measure replace the support which the heart has lost by the stretching and loss of tone of the pericardium, so that aspiration, under such circumstances, is not advisable. Digitalis in full doses often brings relief.

If there is good evidence that the effusion itself is the cause of embarrassment of the heart, there should not be any hesitation in doing *aspiration*. Sometimes this is delayed too long to be of use. There are various possible sites for the puncture; probably the fifth interspace outside the left nipple line is the most satisfactory as a rule. If the exudate is *purulent* prompt drainage is imperative; if effective it gives relief at least for the time. Unfortunately, drainage may become obstructed by adhesions.

CHRONIC PERICARDITIS—ADHERENT PERICARDIUM

Etiology and Pathology.—The most common cause of adhesion of the pericardial surfaces is inflammation caused by rheumatic infection. The adhesion may be partial or complete. If the inflammation is arrested,

little, if any, disturbance of the heart's action will follow, since the pericardium is so loosely attached to surrounding structures that it yields easily to systole and diastole. But if the inflammation persists, however mildly, there will be production of fibrous tissue in the pericardium, and if the inflammation extends into the surrounding tissues so will the formation of fibrous tissue. This process continues as long as the inflammation persists, and may affect the whole mediastinum converting it into a dense mass. Even then the process may not be arrested; the inflammation, in occasional cases, penetrates the diaphragm and infects the peritoneum, the capsule of the liver and even the liver itself. The pleuræ may also be infected.

Other infections may also be the cause of pericardial adhesions. Of such probably tuberculous infection is the most frequent, whether direct or by extension from tuberculous mediastinal glands. Any septic organism may also be the cause of the inflammation.

Irrespective of the nature of infection, the inflammation may slowly extend without symptoms or signs and give rise to an equally slowly progressive fibrosis in the mediastinum. Analogous processes occur not rarely in the lungs following epidemics of pneumonia due to pneumococci, streptococci or influenza bacilli, especially the latter. In the liver and kidneys fibrosis is frequent, in some cases due to a low type of inflammation, although atrophic changes may play a large part.

As the mediastinal fibrous tissue becomes more firm it not only lessens the free action of the heart but binds it to all surrounding structures; the sternum, costal cartilages and ribs in front; the spine, aorta, bronchi, etc., behind; the pleuræ and lungs on each side, and the central tendon of the diaphragm below. As these attachments in time become more and more rigid, increasing strain is thrown on the heart in systole, from which hypertrophy and usually dilatation will result. Hypertrophy is usually marked, especially in early age, when the heart may attain an enormous size if its muscle tissue has not been much damaged by the original infection. Dilatation results in proportion to the cardiac damage that has occurred.

At the same time the veins entering the right auricle may suffer constriction or traction by the newly formed fibrous tissue and impede the entering blood stream; one or other vena cava may be completely occluded. The aorta and pulmonary artery are liable to suffer also but usually to a less degree. Traction by adhesions may affect the systolic and diastolic changes of the aorta, and reduce the force of the flowing blood. If the venous flow into the right auricle is obstructed or impeded there will be venous stasis with the usual results such as enlargement of the liver and spleen, œdema, dropsy, etc.

In occasional cases, the inflammatory process extends to the pleuræ and peritoneum and causes great thickening, especially in the latter — *polyserositis*. The capsule of the liver may become greatly thickened, and fibrous tissue may extend from the capsule into the liver and cause *pseudo-cirrhosis*. The peritoneum may become greatly and irregularly thickened over the liver, the so-called *iced-liver*. Ascites is usually present and may be large, as may also pleural effusion. In time marked œdema

of the legs and abdominal wall takes place. If the superior vena cava is constricted the upper part of the trunk and the arms become œdematous.

Symptoms and Signs.—Adhesion of the pericardial surfaces, of itself, even if general, may not cause any perceptible symptoms or signs, since the attachments of the pericardium to the surrounding structures are sufficiently loose to allow free movement of the heart. But if there is a slowly progressive production of fibrous tissue in the pericardium and invading the mediastinum, due to chronic persistent inflammation, the action of the heart and lungs becomes increasingly disturbed as new fibrous tissue is formed.

Owing to these conditions dyspnœa is a constant symptom, and usually some cyanosis, due to both the lessened respiratory capacity and the hampered circulation. There is little, if any, pain, but, in rare cases, angina pectoris occurs; it may be severe, and excited by slight causes, as movement and excitement.

The *physical signs* are numerous and of great variety. The heart may be greatly enlarged, so much so as to cause fulness of the left side of the chest. The most significant sign is *systolic retraction* of the lower left chest, the intercostal spaces, ribs, costal cartilages and lower end of the sternum. As the heart is firmly attached to the rigid spine, it is enabled to bring the full force of its systolic traction on the lower part of the anterior wall of the chest. Retraction of the intercostal spaces may, however, be caused by a greatly dilated right ventricle, especially if there is compression of the inner triangular part of the left lung. In this case the retraction varies with respiration, but not in the case of adhesions.

In some cases there is also retraction of the tenth and eleventh intercostal spaces below the left scapula and this, if it is not affected by respiration, is evidence of extensive adhesions of the heart to the diaphragm (Broadbent). Similar retraction occurs in compression of the lungs by an enlarged heart, but it varies in respiration.

The *veins* of the neck may be distended in inspiration and suddenly collapse at the beginning of ventricular diastole. Friedrich¹ attributed it to the enlargement of the thorax by the sudden springing back of the ribs, drawn inward by the systole of the adherent heart, making room for the inflow of the blood dammed back in the veins.

Broadbent has observed systolic collapse in the superficial veins on the anterior surface of the chest; he attributed it to the traction of fibrous tissue extending from the pericardium to the internal mammary veins, dragging in and opening them during systole, and obstructing and causing sudden distention of these veins during diastole. Distention of the cervical veins during inspiration is not rare; it is due to pericardial adhesions which prevent dilation of the right auricle (Kussmaul's sign).

On palpation there is perceptible *enfeeblement* or, it may be, *disappearance of the impulse of the heart* in some cases. It is not, however, distinctive of adhesion, as it may occur also in myocardial degeneration, in pericardial effusion, and with changes in position of the anterior border of the left lung. Owing to the adhesions, the position of the impulse of

¹ *Deutsch. Arch. f. klin. Med.*, 1865, 1, 241.

the heart does not alter with change of position of the patient or with respiration. This and fixation of the outline of precordial dulness in respiration are signs of much importance.

Duroziez insisted "on the necessity of considering together the sign of retraction observed on inspection, and the simultaneous shock of systole observed on palpation as affording a diagnostic sign of much value."

Shock, synchronous with diastole, can be felt in occasional cases over the area of cardiac impulse. It is probably due to the rebound of the fibrous adhesions put on the stretch during the heart's systole. By some observers it is regarded as pathognomonic.

The *pulsus paradoxus* is a sign of value. The pulse, if at all affected by respiration, normally becomes slightly fuller and stronger toward the end of inspiration. The paradoxical pulse grows weaker and smaller, and may even disappear, in deep inspiration, regaining its usual volume at the close of expiration. It "is of value in the diagnosis of indurative pericarditis only when there is a concomitant inspiratory engorgement of the jugular veins, a symptom which indicates a *stenosis* of them during inspiration" (Sahli).

On *auscultation* the heart sounds will be found weakened, except during the period of cardiac hypertrophy, when they are usually distinctly accentuated. In mediastino-pericarditis fine friction rales of a parchment-like character are sometimes audible along the margin of the lungs at their junction with the area of superficial cardiac dulness; if they persist during cessation of respiratory movements they furnish strong proof of the existence of pleuropericardial adhesions. A creaking sound over the body of the sternum is, in some cases, audible during up-and-down movements of the arms (Babcock). In some cases a bruit is heard resembling the harsh sound of a presystolic murmur (Hale White).

In cases of "*pericarditic pseudo-cirrhosis of the liver*" and "*multiple serositis*," there is increasing dyspnoea and great ascites, and, later, dropsy of the legs. There may also be effusion into the pleural cavities. There may be a similar group of symptoms without chronic inflammation of the peritoneum; in these cases the pseudo-cirrhosis must affect the portal circulation. In such cases there may be *portal hepatic cirrhosis*, the diagnosis of which is possible only by the symptom group, especially the early appearance of ascites and much later œdema of the legs. The history is also of importance.

Diagnosis.—In well-defined cases there is usually no difficulty. Such a case was that of a lady, aged thirty-five years, who five years previously had a severe protracted pericarditis and recurrences of milder attacks. She made a slow and incomplete recovery, palpitation and dyspnoea on exertion persisting and growing more pronounced. On examination, a well-marked systolic retraction was found to occur in the lower precordial region, affecting the fifth, sixth and seventh costal cartilages and lower end of the sternum, but chiefly in the intercostal spaces and the epigastrium between the left costal margin and the ensiform cartilage. There was no respiratory movement of the epigastrium. The area of dulness extended from the right margin of the sternum to $\frac{1}{2}$ inch outside of the left nipple line, and was not altered by respiration or change of position.

There was a systolic shock synchronous with the recession, but no diastolic shock could be perceived. There was, in this case, the history of such recurrent attacks as would probably cause, not only adhesion of the pericardium, but also infection of the myocardium on the one hand, and of the pleura and mediastinal tissues on the other; none of the essential signs of chronic fibrous mediastino-pericarditis were wanting.

The symptoms are those of failing circulation with evidence of dilatation of the right ventricle without adequate cause to account for it. A protracted history of recurrent pericarditis is significant; and, if the patient has been under observation, the recurrence of inflammation may have been shown by the appearance of friction rubs at various points from time to time, together with an increase of the area of precordial dulness which remains undiminished after the pericarditis has been relieved. In such a condition pericardial effusion must be excluded, and due allowance must be made for dilatation of the heart.

In pseudo-cirrhosis of the liver with general serositis, the diagnosis is often difficult, especially in differentiating it from ordinary hepatic cirrhosis. In the latter affection there is usually a history of a cause such as alcoholism or syphilis, while in adherent pericarditis and multiple serositis there is often a history of rheumatic fever with, in some cases, pericarditis, or an acute illness in which precordial pain, distress, and other symptoms which may have been due to pericarditis were present. In ordinary cirrhosis there are often gastric or intestinal hemorrhages, and the dropsy begins as ascites, œdema of the legs following later; in the pericardial cases the œdema may precede the ascites, the changes in the liver and serous membranes being of later development.

"Great dilatation of the heart without hypertrophy, and not due to disease of the cardiac orifices, nor to lesions of the lungs, kidneys, arteries, stomach, etc., is probably caused by adherent pericardium" (Potain). In such conditions, however, myocarditis is always present, and must be a contributing factor.

Prognosis.—This is usually grave; yet some have periods of great improvement in the serious symptoms. Rheumatic adhesive pericarditis has been regarded as the usual cause of cardiac failure in children, but it is probably more often due to myocarditis, to which they are so liable. The gravity of the condition is greatly increased by the liability to recurrences of the pericardial inflammation, and by the coexistence of endocarditis and valvular affection. The occurrence of chronic inflammation of other serous membranes—polyserositis—and extension of the inflammation to the mediastinum greatly increase the gravity of the prognosis. When the signs of cardiac failure, such as anasarca and ascites, develop, restoration of cardiac competency is difficult to establish and a fatal ending usually comes with a few weeks or, at most, months.

The disappearance of the systolic retraction is of grave omen, as it indicates progressive enfeebling of the heart's energy. The failure of the heart to respond to digitalis indicates profound alteration of its muscular tissue, and adds to the gravity of the prognosis. Death usually results from myocardial failure, sometimes after the first, more often after a succession of crises; it may occur with symptoms of syncope or of an anginal attack.

Treatment.—This is preventive and symptomatic. All rheumatic attacks in children, however, slight, should be carefully treated, prolonged rest in bed after each illness being especially desirable in order if possible to prevent damage to the heart or its membrane. Cold or hot applications, or small blisters to the precordium, may relieve symptoms. Digitalis in moderate doses may do good; it should be continued for long periods. Respiratory gymnastics, by stimulating the heart's action, also aid in lessening the tendency to adhesions.

Once the adhesions are established, the treatment has for its chief aim the development and preservation of the cardiac hypertrophy. To this end the heart should be guarded from overstrain. This calls for the intelligent coöperation of the patient, who should therefore be carefully instructed, without unduly alarming him, as to the dangers and how best to avoid them.

The secondary effects from venous congestion of the digestive organs and the kidneys require frequent recourse to active cathartics to reduce fulness of the portal system. The diet should be nutritious and of small bulk so as not to overtax the digestive organs.

For pain and restlessness in adults, morphine may be given; it is also the best tonic for an overstrained, irritable heart. Anasarca may require drainage.

In cases of marked systolic retraction of the costal cartilages and lower end of the sternum, separation of the adhesions has been proposed by Delormé. Brauer carried out a much more extensive operation, "cardiolysis," consisting in resection of the ribs and cartilages, and even the margin of the sternum, to which the heart and tissues about the pericardium are adherent. The periosteum should also be removed. The object is to convert the resisting chest wall in the *regio cordis* into a soft, yielding tissue, so as to allow the heart to contract and dilate with more ease. By this means not only is the heart relieved somewhat of its hampered action, but it may possibly allow the diaphragm to descend in some degree, and increase the respiratory capacity of the chest. At best the operation can do no more than give the heart a moderate degree of relief as its rigid attachments, especially to the spine, cannot be altered.

SYPHILIS OF THE PERICARDIUM

The *pericardium* is so rarely the seat of syphilitic infection, and the few cases in which infection occurs show such indefinite, if any, symptoms, that the subject is of academic interest rather than one of practical medicine. Ricord, in 1851, was the first to describe the condition; in his case there was some fibrinous exudate on the pericardium. Virchow, in 1861, described the second case recorded; in this case there was adhesion of the pericardium. In 1897, Phillips collected 25 cases of syphilis of the heart and in 5 of these the pericardium was involved.

In nearly all the cases published the pericardial lesion has occurred in association with syphilitic disease of the subjacent muscular tissue. As a rule, only the visceral pericardium is affected and the lesion is usually a circumscribed inflammation, rarely a gummatous deposit. Beneath

the inflammatory areas fibrosis of the muscular tissue is usually found, or a gumma imbedded in the wall of the heart. The parietal pericardium in contact with the affected visceral layer may become infected. The vessels of the affected pericardium are hyperemic, but as the new cicatricial tissue is organized and contracts, they become obliterated and a white scar results. Fluid exudate is rare so that its presence, whether serofibrinous or hemorrhagic, is indicative of tuberculous rather than syphilitic disease. Gumma of the pericardium is very rare. Marceek found only 3 undoubted cases described; since then no fresh cases seem to have been reported.

Of the pericardial lesion itself there are probably no *symptoms*; the disease of the myocardium, with which it always appears to be associated, can, no doubt, cause all the symptoms that may be present during the course of the pericardial affection. A pericardial lesion may be suspected in a syphilitic case that shows signs of a cardiac affection, but its existence can neither be demonstrated nor excluded. In rare cases, possibly, there may be a friction rub. Syphilis of the pericardium, of itself, can scarcely have an influence on the duration of life, and probably rarely causes any disturbance of comfort. The *treatment* is included in that of the general infection.

HYDROPERICARDIUM

Hydropericardium, or *hydrops pericardii*, is a serous non-inflammatory transudation into the cavity of the pericardium, similar to hydrothorax or ascites but occurring with less frequency. It, however, probably exists, in at least a moderate degree, in all cases of marked hydrothorax. The quantity of serum normally in the pericardium is somewhat indefinite, but there is probably not usually more than sufficient to moisten it, although the amount is doubtless subject to variation. At necropsy there are usually 5 to 10 cc., or even up to 100 cc., of clear, straw-colored, alkaline fluid, containing various salts, urea, and sometimes traces of sugar. Some of the transudate probably escapes at the time of death and possibly for a time afterward.

Etiology.—The causes of hydropericardium are either local and of a mechanical nature or general from blood changes as in cachectic states and nephritis. Of the former are such as impede the pericardial circulation, such as lesions of the heart and lungs and local affections, as neoplasms and fibrosis in the mediastinum, which may obstruct the veins of the pericardium, and hydrothorax with which it is nearly always associated. The general causes are the anemias, nephritis, tuberculosis, carcinoma, malaria, leukemia, etc. In these cases the pericardial dropsy is usually associated with dropsy of other serous cavities.

Symptoms.—The symptoms usually develop gradually and its occurrence is usually overshadowed by the causes on which the effusion depends. When the collection of fluid becomes considerable, it causes enfeeblement of the impulse and sounds of the heart, increase of the area of precordial dulness, and sometimes fulness of the precordium. There is no friction rub. If there are no pericardial adhesions, the area of flatness on percussion is modified by respiratory movements and changes of position of the

patient, especially on his assuming a stooping posture. In cases of marked emphysema, the area of dulness is difficult to determine, and is little affected by position. There is no fever or pain. Rapid effusion may cause precordial distress and a feeling of thoracic constriction, with dyspnoea, and disturbance of the action of the heart; in these cases, some affection of the substance of the heart is probable. The effusion may be terminal and rarely recognized.

Diagnosis. A diagnosis is to be made on the basis of the signs of effusion into the pericardium without the symptoms of pericarditis, and the coexistence of fluid accumulation in the other serous cavities, of general dropsy, and of venous stasis. A consideration of the etiology is important. Often, however, it is difficult to differentiate hydropericardium and chronic pericarditis without febrile reaction occurring in nephritis or tuberculosis. The error is not of material importance.

Prognosis.—The prognosis is usually to be measured by that of the affection on which it depends. The debility may be so marked that the effusion may itself endanger life.

Treatment. The treatment is directed to the primary disease to which the hydropericardium is due, tuberculosis, chronic malaria, nephritis, or the state of cachexia. Diuretics, hydragogue purgatives, and diaphoretics are seldom effective and increase debility. When the exudate is large, aspiration gives relief but it is, as a rule, only temporary, as reaccumulation is usually rapid; it is, however, rarely called for, as the patient generally suffers chiefly from the primary affection, and only in a slight degree from the hydropericardium.

HEMOPERICARDIUM

Etiology.—The causes of hemorrhage into the pericardial cavity may be traumatic, as by penetrating wounds, rupture of the pericardium or a coronary artery by crushing injuries and penetration by a fractured rib. Among the internal causes is rupture of the heart during strain or spontaneously; in such cases there is degeneration and perhaps aneurism of the wall of the heart; rupture of an aneurism of the coronary artery may be the cause. A small perforation of an aneurism of the ascending part of the aorta occurs and the blood may burrow its way down between the coats of the aorta and force its way into the pericardial cavity. The more rapid the escape of the blood the less will be the quantity, as the result is quickly fatal; the quantity of blood may not exceed 6 or 8 ounces. If the hemorrhage is slow the patient survives a relatively long time and the volume of blood may greatly distend the pericardium. Rolleston describes a case with a pinhole opening in the external coat of the aorta in which there were 24 ounces in the pericardium, and Mansell Moulin, a traumatic case with recovery, in which 6 pints were removed in the course of several hours. The blood may be fluid, or coagulated, wholly or only in part. In a case of Whittaker's several layers of coagulated blood were stripped from the pericardium, the blood having escaped through a rupture in the heart.

Symptoms.—The symptoms vary with the rapidity of bleeding. If rapid, death is sudden and due to the sudden fall of cerebral blood-pressure; if less rapid, death may be due to compression of the heart and the consequent cerebral anemia. If the escape of blood is slow, there are the physical signs of pericardial effusion with the general symptoms of internal hemorrhage. The onset may be with a sharp pain or a feeling of something having given way.

Diagnosis.—The diagnosis is usually difficult, and often only correctly made at necropsy. Following injuries, it may be evident from the nature of the cause. The diagnosis may be made if there are the signs of sudden pericardial effusion and of internal hemorrhage.

Prognosis.—The prognosis is always grave, and usually hopeless, death occurring at latest within a few days. In traumatic cases with moderate hemorrhage and an injury not necessarily fatal, recovery may take place, but cases due to rupture of the heart or of an aneurism, are necessarily fatal, although life may be prolonged several days. Travers reports a case of extensive traumatic rupture of the right ventricle in which death did not occur until the eleventh day.

Treatment.—The treatment in rapidly fatal cases is wholly ineffective. Ordinarily it should be directed to the cause and to counteracting the effects of the loss of blood. Suturing the wound of the heart has been successful in some traumatic cases.

PNEUMOPERICARDIUM

The presence of air or other gas in the pericardium is very rare and seldom exists without inflammation of the pericardium. The exudate may be sero-fibrinous, purulent or hemorrhagic. W. B. James, in 1904, found only 37 cases recorded in the literature; he added one of his own.

The most frequent cause of gas in the pericardial sac is the entrance of air through a wound due to a stab or gunshot. From internal causes, air may enter through a puncture by a foreign body in the œsophagus or a fractured rib; a crushing injury may lacerate the lung and pericardium and allow air to enter from the torn lung. One or other of these causes account for 18 per cent. of the 37 cases. Pericarditis is always associated with pneumopericardium, and as the germs are usually pyogenic the inflammation is nearly always purulent. Mueller is said to have met with a case of serous exudate, and Stokes reports a case of acute pericarditis followed by hydropneumopericardium with cure.

Gas from various hollow viscera may enter the pericardium through perforation caused by ulceration, as a gastric ulcer perforating the diaphragm and adherent pericardium; subdiaphragmatic abscess opening into the stomach or intestine, and through the diaphragm and adherent pericardium; cancer of the œsophagus; a suppurating cavity in the lung, gangrene of the lung or pneumothorax. These causes accounted for 15 cases. Of the remaining 5 cases, in 4 no opening could be found in the pericardium at the necropsy, so that the gas appears to have been caused by an aërogenous organism. In the remaining case there was

acute pericarditis associated with hydropneumopericardium, with recovery (Stokes).

Symptoms.—The symptoms vary greatly according to the cause and the nature of onset. If the condition develops gradually, the symptoms will be those of a mild pericarditis until the distention of the sac becomes great and causes symptoms of pressure on neighboring organs and functional disturbances of the heart. In the traumatic forms, the entrance of air is sudden and marked by symptoms such as sudden retrosternal pain of a burning character, precordial oppression, palpitation, dyspnoea, cyanosis, and a weak pulse. There may be recurrent syncopal attacks. The symptoms closely resemble those presented by the various forms of pneumothorax. Dysphagia from pressure on the œsophagus has been reported (Eisenlohr).

The *physical signs* are, in most cases, strikingly characteristic. This is shown by the frequency with which the cases were recognized by the observers, nearly all of whom were meeting with the condition for the first time. In only 6 of the 38 cases was the condition not recognized before necropsy. On inspection, the precordial region is prominent, at least in the intercostal spaces, and the cardiac impulse is not visible, but may return with normal force and become visible if the patient assumes the prone position. The percussion sound is tympanitic, of a metallic character, and disappears as the patient assumes the prone position.

As the effusion increases, the lower part of the precordial area becomes flat, the upper remaining tympanitic; with change of position of the patient there is a corresponding change in the relationship of the areas of tympany and flatness. Systole may bring the heart against the chest wall and the note will then be dull. Cracked-pot sounds may be present even without a communication between the pericardium and a bronchus (Stokes). A roentgen-ray examination should give a characteristic picture.

The most characteristic sign of the presence of fluid and gas is the churning, splashing sounds audible over the precordium and synchronous with the heart's action; it was noted in one-half of James' collection under a variety of descriptions, as *bruit de moulin*, *de roue hydraulique*, metallic gurgle, etc. It is of the same character as the succussion sound produced by shaking a patient with hydropneumothorax. Metallic tinkling sounds were heard in 24 cases, also synchronous with the movements of the heart, and usually blended with the churning, splashing sound. The tinkling may be audible at a distance from the patient, who may himself hear it, and be conscious of the tumultuous action in his chest. As the liquid exudate becomes abundant the cardiac sounds are weakened and may disappear; more often they are masked by the various pathological sounds. Precordial friction sounds of variable intensity are frequently heard; in some cases there is a fine crepitation due to emphysema of the cellular tissue in front of the pericardium.

Diagnosis.—This is usually easy on account of the marked and characteristic signs. The condition might be simulated by left pneumothorax and by a large pulmonary cavity in contact with the pericardium. In such conditions the normal outline of the heart, its impulse, and the

arrest of the various churning, metallic, and other sounds on suspending respiration would be diagnostic. Gaseous distention of the stomach sometimes causes metallic heart sounds, but the cause should not be difficult to determine. Confusion with pneumopericardium should not occur if the existence of the normal area of heart dulness, the cardiac impulse, and the absence of material functional troubles and disturbances of the heart are taken into consideration.

Prognosis.—This is grave at best. Of the 37 cases collected by James, 26 terminated fatally and 11 in recovery. In 8 of the 26 cases nearly all the causes of the pneumopericardium would be in themselves fatal; they were such as cancerous and other perforations of the œsophagus, gastric ulcer and subdiaphragmatic abscess perforating the diaphragm, and tuberculous ulceration and gangrene of the lung opening into the pleura and later into the pericardium. The relatively large number of recoveries shows that the heart is remarkably tolerant of pericardial disease, that is, so long as its own substance is not involved. Much may depend on the suddenness of the distention of the pericardium with gas, as shock will be induced in the cases of sudden development, and add greatly to the danger.

Treatment.—This should be prompt. In traumatic cases, the opening should be closed at once by an antiseptic dressing. If an abundant exudate threatens cardiac collapse from compression, evacuation of the pericardial contents becomes necessary. If the exudate is purulent and putrid, the original opening should be enlarged to give free discharge to the exudate. Some advise irrigation with warm antiseptic solution.

If there is shock, stimulation and the application of heat are necessary. Pain and distress should be relieved by morphine hypodermically. Digitalis or strophanthine should be given hypodermically if the action of the heart is depressed.

NEOPLASMS OF THE PERICARDIUM

The various neoplasms of the pericardium are malignant, as *carcinoma* and *sarcoma*, and non-malignant, as fibroma, enchondroma, free bodies and hydatids. Carcinoma and sarcoma may be *primary* or *secondary*.

Primary cancer is very rare and even its occurrence is disputed. Of the cases reported it is not clear how many are cancer and how many are sarcoma. Sir W. Broadbent reported a case of sarcoma of the pericardium in 1882, and Williams and Miller a case of primary sarcoma in a child, aged thirteen years. Broadbent's case was in a stout, florid man, aged twenty-three years, who complained of some discomfort in the lower part of the thorax. For two months he had had pain in the shoulders and down the arms, and dyspnoea on exertion. After the onset of the dyspnoea there were signs of fluid in the left pleura and in the pericardium. Three weeks later there was no fluid in the pleura, but the pericardium was apparently distended and the dyspnoea increased. He was tapped but no fluid was obtained; the trocar impinged on a firm fixed

mass. He died three days later. At autopsy, the pericardium was found $\frac{1}{2}$ inch thick at the base, the thickness increasing upward and $1\frac{1}{2}$ inches at the great vessels. On examination it proved to be sarcomatous.

Secondary growths are scarcely more frequent. In 477 cases of cancer in various parts, in only 7 was the pericardium affected (Willigk). Kobler found cancer 6 times in 9118 autopsies. They may be secondary to cancer of the heart or of some neighboring part, as the mediastinum, the bronchial glands, pleura, lung, or œsophagus. It is sometimes involved in cases of generalized metastatic nodules secondary to cancer of distant organs. In it are reproduced the anatomical characters of the original disease; this is true of sarcomatous growths also. They always give rise to pericarditis with more or less effusion, which may be serous, oftener hemorrhagic, and sometimes purulent or even putrid. In some cases the invasion occurs as a diffuse infiltration, affecting more or less extensively the serous membrane and subjacent tissues; in others, the disease occurs in the form of distinct growths.

Symptoms.—The symptoms are those of mild or chronic pericarditis with the general, grave condition usually occurring in malignant affections. The subclavicular glands may be involved and render the diagnosis quite clear. If aspiration is rendered necessary by the abundance of the effusion, a hemorrhagic fluid is usually obtained; it is, however, occasionally purulent and even putrid. There may be the signs of primary or secondary carcinoma elsewhere.

The *diagnosis* is indicated by malignant disease in other parts of the body. In the absence of such growths the diagnosis may be impossible. It may simulate pericardial effusion.

The *prognosis* is necessarily fatal and the duration brief.

The *treatment* is wholly symptomatic, the objects being to relieve distress and maintain strength. If the effusion is abundant, aspiration will be necessary; it is questionable if free drainage will be desirable, even if the exudate is purulent.

Various Neoplasms.—Occasional reference occurs in the literature to non-malignant neoplasms in the pericardium. Bouchard reported a case of polypus in a child aged four years. Free bodies in the cavity of the pericardium have been found; they owe their origin probably to polypi. They may consist of soft tissue or of firm, fibroid structure, and are occasionally calcareous (cardioliths).

Fibroid tumors and *lymphomas* of the pericardium have been reported, and 1 case of cystic enchondroma has been met with.

Bouchard described fringes resembling those met with at times in the knee and other joints. They may be pedunculated or even become free, forming soft, foreign masses. Foreign bodies may also arise from a coagulum of fibrin or from inspissated pus in which lime salts have become deposited.

Hydatids of the pericardium are very rare. The late Davies Thomas of Australia, found the record of only 2 cases. Others have been reported by Barlow, Enos, and Rapp, Chadzynski, Bernheim, and MacDonald. In Chadzynski's case the cyst was very large and ruptured into the peri-

cardial cavity. Hydatid cysts of the pericardium present no symptoms of special significance. As a rule, hydatids coexist elsewhere and may guide to a correct diagnosis.

ABSENCE OR DEFECT OF THE PERICARDIUM

Absence of the pericardium is rare; it is usual in cases of serious anomaly, such as ectocardia, etc. Partial defect is more frequent, the pericardium usually taking the form of a falciform fold projecting upward from the diaphragm and forming an incomplete pericardial sac. Bristowe described a specimen which consisted of a rudiment of the pericardium at the upper and right side of the heart. In 1 case of incomplete pericardium, death resulted from dislocation of the heart during a severe attack of vomiting.

Sir Arthur Keith¹ reports cases of partial deficiency of the pericardium; the deficiency is always on the left side, and the phrenic nerve had a distinct relation to the opening which he regards as a patent pleuro-pericardial foramen.

Chylous and *chyliform* effusions into the pericardium are extremely rare.

¹ *Jour. Anat. and Physiol.*, London, 1907, **11**, 3rd Ser. ii, 6.

CHAPTER XIV

THE RATE AND MECHANISM OF THE HEART BEAT

By SIR THOMAS LEWIS, M.D., F.R.C.P.

Historical and Introductory.—Modern conceptions of heart irregularities have originated from the physiological work of the late seventies and eighties. Although the heart beat had been regarded by Haller as a peristaltic wave of contraction, passing from the venous inlet to the arterial outlet, yet this view found no general acceptance until after the experiments of Gaskell, MacWilliam, Engelmann and others.

It has been shown that the beat of the ventricle is initiated by the contraction of the auricle and that in the cold-blooded heart, where the sinus and auricle are clearly delimited, the auricle receives its impulse to contract from the sinus region. The work upon the frog and tortoise heart was quickly followed by similar observations upon the mammalian heart, and attention became focussed upon the anatomy of those regions of the mammalian heart where auricle joins ventricle, and where sinus remains were supposed to exist.

Knowledge progressed to the discovery of two clearly differentiated structures in the mammalian heart; the auriculo-ventricular conducting system, which forms the functional union between auricles and ventricles, and the sino-auricular node, lying near the mouth of the superior vena cava; the heart beat is now known to arise in this node. The modern conception of the heart beat is based upon extensive study of the anatomy, physiology, and morphology of that organ, and a certain familiarity with these studies is essential to the correct understanding of normal and perverted heart mechanism. The controversy between those who have advocated the myogenic or the neurogenic origin and transmission of the contraction wave has had a conspicuous influence upon the trend of observation. These rival hypotheses have prompted the discovery of many new facts. The myogenic doctrine, according to which the heart beat arises in a muscle cell and according to which the impulse is conveyed through muscle fibres, is the more generally accepted; but it is unfortunate that this theory, now ascendant, has become associated with a doctrine of manifold function of heart muscle.

The strict separation of the five cardiac functions—rhythmicity, contractibility, excitability, conductivity, and tonicity—is one which is jealously guarded by many writers, and more especially by those who have followed in the footsteps of Engelmann. That the heart musculature—and by the term “musculature” I mean the cardiac muscle in full functional connection with its nerves—has these attributes is clear; but that certain of the functions are special attributes of particular regions of the heart, a fact brought into prominence by Gaskell’s writings,

has not received sufficient emphasis by many later workers. The tendency of some clinicians to class disorders of the heart beat according to perversions of one or other of these so-called functions is unfortunate.

If the controlling cardiac impulses are initiated in an abnormal manner, the derangement is to be regarded, not necessarily as a disturbance of the function of rhythmicity, but as a disturbance of the functions of the special tissue lying in the region of the superior vena cava, and known as the sino-auricular node. Similarly, disturbances in the transmission of the contraction wave in its progress from auricle to ventricle are often to be regarded, not as a disturbance of conductivity, but rather as a derangement of those special tissues forming the paths through which the contraction wave flows. A clearer conception may be formed if the disorders subsequently to be spoken of as auriculoventricular heart-block are instanced.

To describe dissociation between auricles and ventricles as a disturbance of conductivity, using this word in its special sense, is misleading. The disturbance is often brought about by complete transection of the tissues uniting the two chambers. Under this circumstance we clearly deal not with disordered function, but with structural damage. Again, the classification of premature contractions or extrasystoles as disturbances of excitability is not warranted by our knowledge of the former or by our definition of the latter. Excitability of any region of the heart is defined as its property of responding to artificial excitations, mechanical, chemical or electrical. We have no evidence that the excitability is raised in those hearts which give rise to the new beats; we have some evidence to the contrary. Whatever may be the value of separating and isolating the normal cardiac functions, the division forms but an insecure foundation in classifying disorders of the heart beat at the present time. The classification adopted in the present chapter is based upon the simple facts at our disposal rather than upon a hypothesis which may prove unfounded.

As it is to experiments upon animals that we owe our knowledge of the normal heart mechanism, so it is mainly to similar experiments that we look for our earliest acquaintanceship with disordered mechanism. To the names already given those of Erlanger, of Hering and many others might be added. But the knowledge of perverted action in animals could never have been applied to the human subject but for further enterprise. The correlation of experimental and pathological facts has been facilitated by a number of workers. Cushny and Wenckebach have the credit of first comparing the clinical irregularities of the ventricle with those induced experimentally; Mackenzie and Einthoven by elaborating special graphic methods have given us ready means of recording the movements of the different chambers of the heart.

The sino-auricular node (of Keith and Flack) in the human heart is a small neuromuscular organ lying in the upper reaches of the *sulcus terminalis*, near the junction of the superior vena cava to the right auricle. The muscle of this important structure consists of fine spindle-shaped interlacing fibres, imbedded in a dense meshwork of connective tissue and richly supplied by nerve elements (especially, on the inhibitory

side, by fibres of the right vagus). In it the normal heart beat originates, spreading to both auricles and to the junctional tissues at the auriculo-ventricular ring.

The *auriculo-ventricular junctional system* has its origin in the septum of the auricles where small muscle fibres collect fanwise to a centre and eventually interlace to form a second node, the auriculo-ventricular node (of Tawara). This node has a similar structure to that previously described and is also richly endowed with nerves. It is continued as the auriculo-ventricular bundle (the bundle of Kent and His), which after piercing the auriculo-ventricular ring and approaching the upper borders of the membranaceous septum breaks into two main branches, right and left, respectively. The main branches course along the septal walls of the corresponding ventricles and, breaking into a complex arborization (the network of Purkinje), are distributed to the ventricular muscle. This system possesses the function of carrying and distributing those impulses which descend from auricle to ventricle. Thus the rhythmic impulses arise in the sino-auricular node under the governance of the great heart nerves; they awaken contractions in the auricles and these in their turn send messengers to the ventricles, again under the governance of the great heart nerves, and through the medium of the special structures described. Such is the simple plan of the rhythmic and coördinate heart beat as we know it. But the junctional tissues between auricle and ventricle subserve at least one other function: they act as subsidiary centres, from which, in the time of need, rhythmic impulses are elaborated and sent to the ventricles. Like the sino-auricular node they are specially endowed with the power of awakening heart beats, and this property is called into play when the union between auricle and ventricle is disturbed.

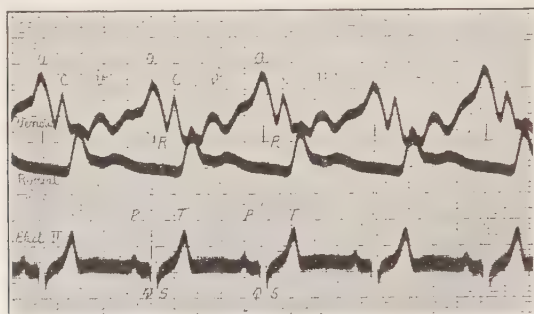
Polygraphy is a mechanical method of obtaining separate and simultaneous records of the auricular and ventricular contractions. As ordinarily practised, a curve (Fig. 16) is taken from a large artery, another from the veins at the root of the neck; the first signals the movements of the left ventricle (and, as the two ventricles beat together, of the right ventricle also), the second signals the movements of the right auricle (and, as the two auricles beat together, of the left auricle also). When the normal sequence of contraction is disturbed the disturbance is analyzed by identifying the instants of contraction in the two main subdivisions of the heart (auricle and ventricle) relative to each other. It is essentially a bed-side method.

Electrocardiography is a method practised with similar objects in view, but it is of far greater accuracy and takes the analysis further. Besides recording the separate contractions in auricle and ventricle (Fig. 16), it throws definite light upon the *direction* of contraction in the muscle of the separate chambers.

As an accompaniment of systole in auricles or in ventricles, electric energy is developed in the heart, and is diffused throughout the whole body. It is tested in the limbs, which are connected to a suitable and highly sensitive galvanometer. With each normal heart cycle the auricles yield currents, which change in amount and direction; so, too, in

the case of the ventricle; these currents flow through the instrument and are recorded by it. Each subdivision of the heart gives its own curve, a curve characteristic of normal contraction; for the shape of the curve is controlled by the direction of the excitation wave in the muscle giving birth to it. Suitable experimentation allows the direction of contraction, normal or abnormal, to be identified.

FIG. 16



Simultaneous curves taken by a photographic method. $\times \frac{2}{3}$. Venous, arterial, and electrocardiographic curves are shown. The vertical lines mark fifths of a second in these and subsequent figures. The horizontal lines are at millimeter distances, and the electrocardiograms are so standardized that one millivolt corresponds to 10 millimeters on the scale. Any vertical line cuts the three tracings at the same instant in time. In the case of the two mechanical curves an allowance of 0.016 second must be made for time lost in the instrument. The same remarks apply to subsequent and similar figures. The venous curve consists of *a*, *c*, and *v* waves; the wave *c* occurs about one-tenth of a second before the radial up-stroke and is coincident with arterial pulsation in the neck. It marks the onset of ventricular systole in the venous curve. Preceding it is a wave *a* falling in presystole and resulting from the contraction of the auricle. Lastly, the summit *v* occurs opposite the bottom of the dicrotic notch in the arterial curve, the wave marks the end of ventricular systole. In the electrocardiogram, *P* corresponds to systole in the auricle; the deflections *Q*, *R*, *S*, and *T* correspond to ventricular systole. The auricular and ventricular events in the electrocardiogram precede similar events in the jugular curves by a little more than one-tenth second. This difference is due to (1) the appearance of the electric effects very slightly before sensible contraction in the muscle (about 0.02 second), (2) delay in transmission of the venous waves from the auricle to the neck (about 0.10 second), and (3) delay in the transmission of venous waves through the recording instrument (about 0.016 second).

Pathological Types of Disordered Mechanism.—The chief types of disordered heart mechanism may be described under the headings which succeed. They are:

1. Disturbances of impulse production.
2. Heart-block.
3. Premature contractions or extrasystoles.
4. Simple paroxysmal tachycardia.
5. Auricular flutter.
6. Auricular fibrillation.
7. Alternation.

1. **Disturbances of Impulse Production.**—The disturbances of heart-action which fall under this heading are broadly three in number, namely, increase of rate (simple tachycardia), decrease of rate (simple bradycardia) and irregular action ("sinus irregularity"). In each and all of these

states the sequential action of the separate chambers is undisturbed; the impulses creating contractions all arise at the natural pace-maker or sino-auricular node, and all the heart chambers are equally and successively involved in the disturbance.

Simple Tachycardia, or Rapid Heart Action.—Simple tachycardia may be produced experimentally in one of three chief ways, (a) by altering the innervation, for example by section of the vagi, by administration of atropin, or by stimulation of the sympathetics; (b) by altering the chemical environment of the pace-maker, for example by acidifying the blood or by the injection of adrenalin, salts of sodium, etc.; (c) by altering the physical environment, a notable example of which is the reaction to increased temperature.

In the human subject, simple tachycardia is seen in a variety of conditions and the exact manner of production is often unknown. The heart rate may be persistently far above the average (to 100) as a physiological variation in the healthy subject. The rate is much faster in children than in adults, it increases with exercise (to 180), with mental effort or excitement, and with the application of heat to the body. It is increased by fever and in all acute febrile diseases; though to a lesser extent in those which affect the central nervous system and in typhoid fever. Simple tachycardia is prominent after hemorrhage and shock. It follows lesions of the vagi, especially the right nerve, and is a usual and special feature in exophthalmic goitre. Simple tachycardia is often associated with local infections, whether fever is present or not, notably in pulmonary tuberculosis, pericarditis, etc. It occurs in intoxications, especially in belladonna poisoning and in chronic alcoholism. A high ventricular rate is frequent in mitral stenosis, in aortic regurgitation, and in renal disease associated with Cheyne-Stokes breathing (80 to 100). As a temporary disorder, simple tachycardia is often encountered in those who present signs of nervous irritability, giving rise oftentimes to attacks of *palpitation*; overreaction of the heart rate to simple causes is seen in these subjects, in those who are convalescing from acute illnesses, and in those who are the subjects of chronic infection or whose health is generally impaired.

The Irritable Heart of Soldiers and So-called Heart Strain.—The irritable heart of soldiers is a term used originally by Da Costa in describing a condition met with in campaigners of the American Civil War. A persistent tachycardia (90 to 120 or more) was one of the symptoms discovered in a number of soldiers. The patients, often young and raw recruits, submitted to the rigors of a strenuous campaign, underfed, exposed, sufferers from fever, diarrhoea, scurvy and wounds, developed symptoms of palpitation, dizziness, precordial pains and dyspnoea. An abrupt, jerky, and extended impulse, increase of heart rate with or without slight or gross irregularity, paroxysms of acceleration, usually in the absence of murmurs and signs of hypertrophy, constituted the chief signs. The majority progressed to recovery. The group is not a distinct one and in this respect, as well as in others, bears a close resemblance to that of "heart strain" so-called. The pathology of these conditions cannot be held to be special, nor can many of the patients be grouped

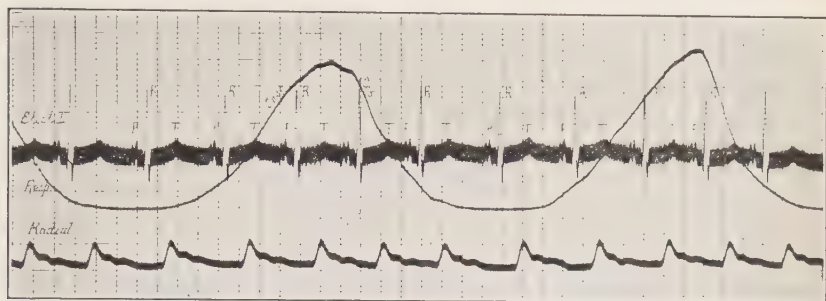
as subjects of primary cardiac disease. Some it is true are described as presenting distinct signs of myocardial involvement, those especially in whom paroxysms of tachycardia and gross irregularity were observed; but such patients belong to groups which we shall consider hereafter, and tachycardia of these types should be rigidly separated from those examples of simple acceleration which are our special consideration in this section. The terms "irritable heart" and "strained heart" are terms which have been used in a comprehensive and loose fashion to cover ailments, the natures of which were imperfectly understood. There is a common misconception that dilatation of the heart produces tachycardia. Direct experiment shows that this is not the case. When dilatation and tachycardia are associated, the dilatation is secondary to the tachycardia or both are due to common or different causes. The term "effort syndrome" was introduced during the period of the Great War as a term which, while conveying a sufficiently accurate idea of patients of this class, namely, those in whom slight effort produces the symptomatology normally following strenuous effort, yet purposely fails to identify any particular system, such as the cardiovascular or nervous systems, as the seat of the original mischief.

Simple bradycardia or slow heart action may be obtained experimentally (a) by altering the innervation, for example by continued stimulation of the vagi, electrically or by the administration of morphia; (b) by altering the chemical environment of the pace-maker, notably by the injection of potassium salts or by prolonged asphyxia; (c) by altering the physical environment of the pace-maker, notably by the application of cold. Slowing of the whole heart is associated with a variety of conditions in the human subject. Although the rate of 72 per minute has long been accepted as an average rate in the normal subject, lower rates (55 to 60 to 65) are not infrequently seen in perfectly healthy individuals. The heart rate is often slower during the last half of the second decade and is frequently below the average in athletes at rest. I have seen a notable example in a perfectly healthy athlete, whose heart-rate while he was quiescent was habitually between 30 and 40 per minute. The rate decreases in adults with advancing years; it may be peculiarly slow during the puerperium. It decreases subsequent to exercise, is often slow in fatigue, and may be retarded by exposure to cold. The heart-rate is often slow during convalescence from acute illnesses. Retardation of the heart may be associated with gross cerebral lesions, more especially tumor, apoplexy and meningitis. It is seen in myxœdema, and is said to occur in the epileptic, in melancholia and hypochondriasis. Jaundice, diabetes and certain forms of uremia (especially if the blood pressure is raised) are often accompanied by it. It is said to occur with notable frequency in disease of the alimentary and genito-urinary tracts.

Sinus irregularities may be defined as irregularities of the heart which are produced by interferences with the rhythmic impulses at the seat of their discharge, namely the natural pace-maker; they are generally due to changes in vagal tone. Sinus irregularities affect all the heart chambers equally, and are of several types. We may consider the three most important:

(a) *Respiratory Irregularity.*—In dogs, a waxing of heart rate with inspiration and a waning with expiration are prominent and normal phenomena. The same irregularity is often, if not usually, encountered in perfectly healthy children, though the degree in which the heart rate changes is less; in young adults the same periodic change of rate happens when the breathing is deepened (Fig. 17).

FIG. 17



Simultaneous electric, respiratory curves and arterial tracing. $\times \frac{2}{3}$. The irregularity is of sinus origin and is coincident with the phases of respiration as shown on the curve. There is a quickening of the heart rate and pulse rate during the phase of lowered intrathoracic pressure, and a retardation during the phase of raised intrathoracic pressure.

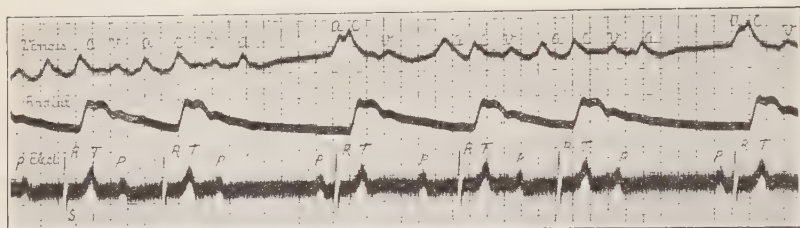
(b) *A sinus irregularity independent of respiration* is met with in some young subjects in health, and also occurs as does the respiratory irregularity when the pulse is slow after exercise and during convalescence from acute illnesses. Both may be produced by digitalis administration. The sinus irregularity is not necessarily periodic, but becomes so if the breathing is deepened and the periods are then synchronous with the acts of breathing.

(c) *Standstill of the Heart.*—Exceptionally, syncopal attacks are the result of cessation of the whole heart beat. The standstill results from vagal discharges and is in every way comparable to the standstill which results when the right vagus is excited experimentally. The clearest clinical instance of this kind has been described by Laslett; others have been recorded by Mackenzie and Wenckebach; Neuburger and Edinger's case, in which an aneurism pressed upon the medulla, probably belonged to the same group. Syncopal attacks may be produced in the healthy subject, as Czermak first demonstrated, by pressing upon the vagus in the neck.

2. **Heart-block.**—Auriculo-ventricular heart-block may be defined as an abnormal heart mechanism in which there is a delay in the response, or an absence of response, of the ventricle to auricular impulses. Normally the ventricle contracts about a fifth of a second after the auricle. Heart-block occurs in two forms; either it is partial or it is complete. If *partial*, then the block may consist (1) simply of a prolongation of the intervals between corresponding auricular and ventricular contractions; (2) of dropped beats (Fig. 18), the ventricle failing to respond to an auricular

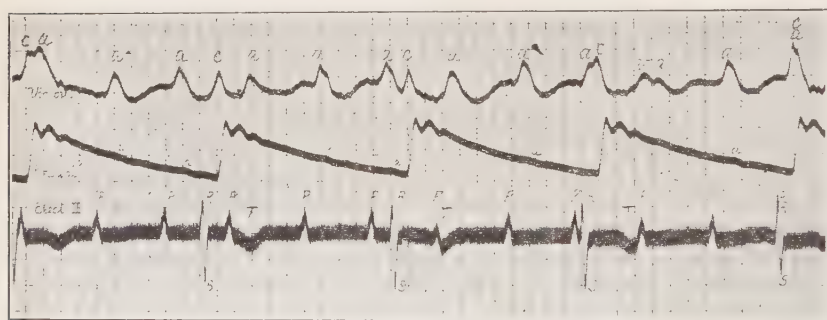
stimulus from time to time; (3) of a reduction of ventricular rate to one-half, one-third or one-quarter, the auricular rate being maintained. In *complete block* (Fig. 19) the auricles and ventricles beat at independent rates, the ventricle elaborating its own impulses (from the junctional tissues) at a rate of 30 or more beats per minute.

FIG. 18



Simultaneous arterial and electrocardiographic curves, showing partial heart-block. $\times \frac{2}{3}$. The *a-c* interval and the *P-R* interval are prolonged to double their normal values, except at the ends of the longest pauses. On two occasions the ventricle fails to respond to the auricular contraction and an *a* wave in the venous curve, a *P* summit in the electrocardiogram, appears in an isolated fashion. The heart-block is responsible for the intermittence occurring at regular intervals in the pulse.

FIG. 19



Simultaneous curves showing complete heart-block, or dissociation of auricular and ventricular contractions. $\times \frac{2}{3}$. The rate of the radial pulse is 27 per minute; the rate of the ventricle is the same; the rate of the auricle is 75 per minute. The relation of auricular and ventricular systoles is especially well shown in the electrocardiogram. The auricular summits *P* occur at regular intervals throughout the whole curve, so do the deflections corresponding to the ventricles (*R*, *S*, and *T*). Opposite and a little later than each ventricular complex (*R*, *S*, and *T*) is a solitary radial pulsation; opposite and a little later than each *P* summit is a wave *a* in the jugular curve, and a minute *a* wave upon the radial curve. Where *a* and *c* fall together, larger waves occur. Note the accurate manner in which auricular and ventricular deflections superimpose when they fall synchronously. In the last cycle, *P* falls upon *R* and *S*; *R* is consequently raised and *S* is less deep.

Heart-block may be produced experimentally in one of three ways. (a) By direct interference with the auriculo-ventricular bundle, which conducts the impulses to the ventricle. Thus pressure upon this tract will, according to its degree, produce varying grades of block (Erlanger).

Firm compression or section of the bundle dissociates the contractions of auricle and ventricle and produces complete block. (b) By stimulation of the vagus, especially the left nerve. (c) By intoxication; for example, by asphyxiation, by the injection of digitalis or an allied drug, or large doses of adrenalin or diphtheria toxin.

In the human subject heart-block may be seen at all ages from birth to old age. It usually results from a demonstrable lesion in the course of the auriculoventricular bundle. The hearts from very many subjects of this malady have received careful examination; very few cases have been recorded in which lesions could not be found in this situation. The lesions appear near the central fibrous body of the heart and in the membranaceous septum; the most frequent being localized gummata or less clearly defined infiltrations or scarrings of syphilitic origin; or simple fibrosis, combined or uncombined with calcareous deposits. An ulcer invading the tract, an endothelioma starting in it, tumors (fibromata, etc.) or necrosis involving this bundle have also been described among other lesions. In acute cases lymphocytic deposits are the rule. Of the infective diseases, rheumatic fever is especially concerned in the production of heart-block; it is also seen in diphtheria, influenza, pneumonia, and typhoid fever.

Heart-block may also result in the human subject, temporarily at all events, from vagal influences; it may be produced by deliberate pressure upon the vagus in the neck. Heart-block when present has been relieved by the administration of atropine and in a few cases lesions of the vagus have been described, though no such case is beyond criticism. Chronic heart-block is probably never to be attributed solely to this cause.

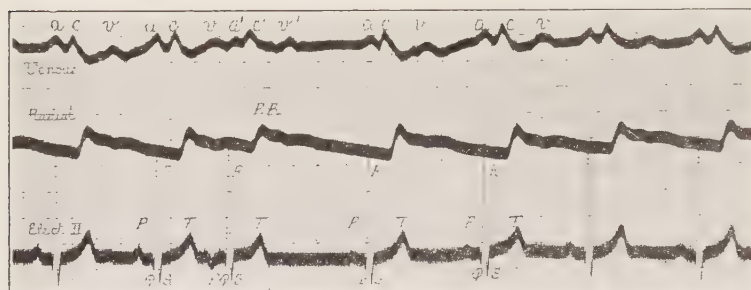
Heart-block also occurs in susceptible subjects during the administration of digitalis, strophanthus and squill.

3. Premature Contractions or Extrasystoles.--Premature contractions are responses of the heart to isolated impulses, thought to be formed *de novo* in the musculature; they are contractions which occur before the anticipated time and which consequently disturb the rhythmic movements of the heart. Actually the nature and derivation of the impulses in question are not understood. Premature contractions are of two chief kinds: some arise in the ventricle, others in the auricle. Arising in the auricle, they spring, not from the pace-maker, but as a rule from some extraneous or ectopic point. The premature auricular contraction is followed by a similar beat in the ventricle (Fig. 20), which, therefore repeats the auricular irregularity. The premature ventricular contraction (Fig. 21), on the other hand, does not usually disturb the sequence of auricular contractions; the disturbance is confined to the ventricle. Premature beats very frequently cause grouped beating of the ventricle, regular alternate beats being premature, or a premature beat occurring after a fixed number of normal cycles (two, three, four, or more). When they fall early in diastole they may not raise the aortic valves, and the pulse rate is then slower than the ventricular rate. Not uncommonly the pulse rate may be halved in this manner.

Experimentally similar disturbances may be induced by applying isolated shocks (electrical or mechanical) to the muscle, by suddenly

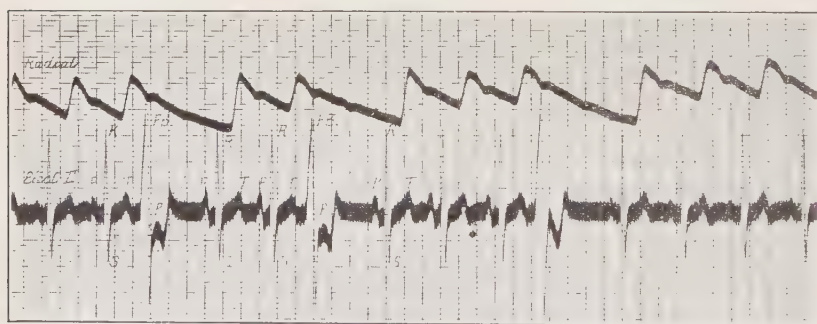
raising arterial pressure (Hering) or by the administration of poisons (notably chloroform in small doses, epinephrine, digitalis, chlorides of barium and calcium, aconitine, nicotine, etc.). They may be caused by producing anemia of the heart, when for instance the muscle is robbed

FIG. 20



Simultaneous curves illustrating a premature contraction or extra systole of auricular origin. $\times \frac{2}{3}$. The normal rhythm is interrupted by an early beat which shows itself in each curve. The arterial curve shows the early ventricular beat; in the venous curve this early ventricular beat is accompanied by c' and v' waves, and c' is preceded by a wave a' , corresponding to the premature auricle. The same events are shown in the electrocardiogram, where the early beat is represented by deflections, P , Q , R , S , and T . The beat arises in some ectopic auricular focus, it spreads in an abnormal manner through the auricle, and consequently gives an abnormal P deflection. It spreads from the auricle in normal fashion to the ventricle and consequently gives normal ventricular deflections, Q , R , S , and T .

FIG. 21



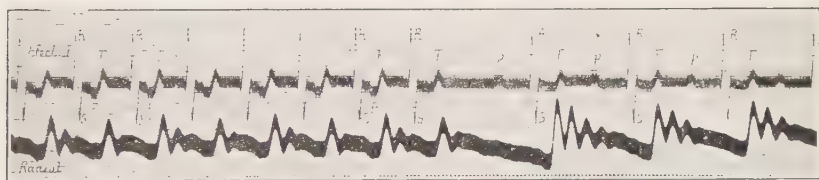
Simultaneous radial and electrocardiographic curves showing premature contractions or extrasystoles of ventricular origin. $\times \frac{2}{3}$. The normal beats of the heart are accompanied by P , Q , R , S , and T deflections. After each second or third normal heart beat, a premature contraction arises in the ventricle; it courses through the ventricle in an abnormal direction and the corresponding ventricular curve in the electrocardiogram is therefore abnormal. Because of its prematurity it is weak and gives rise to no arterial pulse beat. The pulse consequently intermits.

of its blood supply by obstruction of the caval veins or branches of the coronary arteries. If a predisposition to extrasystole formation is awakened, then stimulation of the sympathetic nerves enhances the tendency.

In the human subject extrasystoles are seen in early life as accom-

paniments of infectious disease (diphtheria, especially); in later years they may be associated with almost any disease, infectious or otherwise; they occur occasionally in a large proportion, if not the majority, of healthy adults. When numerous, their incidence is greatest in heart disease. Of the factors which appear to be predominantly associated with numerous extrasystoles, gross lesions of the heart (myocardial disease, coronary disease and mitral stenosis) unquestionably stand first. Excessive tobacco smoking may be responsible. Full doses of digitalis and its allies often induce them. There are clinical associations between premature contractions, raised arterial pressure, anemia of the heart and digestive disturbances (especially flatulence), but these are not fully understood at present. When the heart is predisposed, fatigue is a provocative cause; they are also especially frequent after exercise, when the heart rate slows; mental effort is also spoken of as an exciting cause. There is no special histological anatomy.

FIG. 22



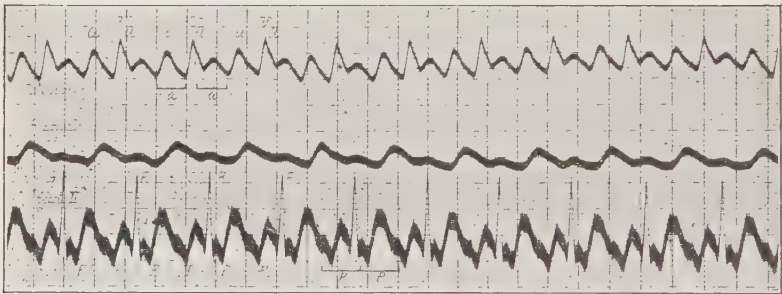
Electrocardiogram and arterial pulse curve showing the termination of a paroxysm of tachycardia. $\times \frac{2}{3}$. In the radial curve the rapid heart action is terminated by a long pause and the normal and slower heart action is then resumed. The ventricular electrocardiograms of the fast and slow period are exactly alike, showing that during the paroxysms the heart beats arose, as in the normal period, from a supraventricular focus. The auricular contractions are to be made out in the electrocardiogram; during the slow period they are of normal outline but the *P-R* interval is increased; during the paroxysm the auricular contraction consists of an inverted deflection which notches the commencement of *T* in each cycle, except the last. Note the alternation of the pulse during the paroxysm. The time marker in this curve is in thirtieths of a second.

4. Simple Paroxysmal Tachycardia.—This is a condition in which from time to time the normal mechanism is abruptly submerged in rapid contractions of the heart chambers, responding to a regular series of new impulses. The normal pace-maker of the heart initiates its impulses at a rate of 72 per minute. If a new centre of impulse formation develops in some extraneous or ectopic focus in the musculature, and the impulses are formed serially and at a faster rate, then the new centre becomes the pace-maker, and dominates the movements of the whole heart. Such is supposedly the condition in simple paroxysmal tachycardia; the paroxysms consist of *sudden* accelerations of heart-rate, and the contractions composing the paroxysm come from a series of new and rhythmic impulses, started in a fresh cardiac centre (auricular or ventricular). The change in the heart-rate, both at the onset and offset of the paroxysm (Fig. 22), is absolutely abrupt. The paroxysms vary in rate between 110 and 200 per minute; they may have a duration of a few seconds or may last a few hours, a few days, or a week or more.

Paroxysms of this kind have been induced experimentally by ligaturing branches of the coronary arteries and by the injection of those drugs which are known to give extrasystoles; the paroxysms are in fact probably composed of extrasystoles, arranged in a regular series.

In the human subject they may be definitely related to posture, occurring only while the patient stands, disappearing when he lies or when on standing the abdomen is compressed; a relation which suggests that they may be provoked by cardiac anemia. In quite half the cases no history of infectious disease is discovered, and in a large proportion of the patients, the heart seems otherwise almost normal. Of past infections rheumatic fever is alone common; occasionally malaria, scarlet fever and measles have been associated with the condition. Paroxysms are fairly common in patients who suffer from heart disease, especially those who show symptoms or signs of myocardial inadequacy and in those who present mitral stenosis. Where there is the predisposition, attacks are induced by exercise and emotion. Flatulent dyspepsia is a frequent association. A special histological anatomy is unknown.

FIG. 23



Venous, arterial, and electrocardiographic curves from a case of auricular flutter. $\times \frac{2}{3}$. The rate of the auricular circus movements and contractions is 250; the rate of the ventricular contractions is 125 per minute. The ventricular contractions are easily distinguished by means of the summits *R* in the electrocardiogram, one of which occurs with each radial pulse beat. The auricular contractions are more difficult to distinguish; they are of very considerable amplitude, amounting to 6 millimeters, and are contiguous, giving to the electrocardiogram a very curious and characteristic appearance. The summits *R* arise from a base line which is constantly moving in a regular zigzag fashion. Each movement of this base line represents a circus contraction, but alternate movements are rather larger, because *T* falls with alternate *P* summits. The venous curve is also a complicated one; each cycle is accompanied by three chief waves, one of these is clearly an *a* wave, the two which occur together are a combination of *v* and a second *a* wave. A more detailed analysis is shown by the brackets underneath the curves.

5. Auricular Flutter.—Auricular flutter is a remarkable condition in which, as has recently been shown, the normal mechanism is wholly in abeyance, and the contraction wave travels in a ring of auricular muscle. The wave completes the same circuit over and over again in this ring, supplying the impulse to the remaining auricular tissue at each of its "circus movements." The number of the circus movements varies in different subjects; it lies between 200 and 350 per minute, the rate of auricular beating corresponding. The ventricle beats at a slower rate

(usually at one-half) (Fig. 23), though, as a rule, in response to the auricle. Acceleration and heart-block are combined therefore. Flutter, which is only known definitely to arise in the auricle, may occur in short paroxysms; but more often it is persistent, lasting for months or years when untreated. It is closely related to a condition presently to be described, namely, fibrillation of the auricles, and often becomes converted into it.

Experimentally it may be produced at times by repeated stimulation of the auricle by means of rapid and rhythmic shocks. Clinically it may be associated with rheumatic heart disease, but usually the heart shows no sign of disease beyond slight enlargement. A recent history of "influenza" has been spoken of in several cases; infections of the urinary tract may be present. Though it occurs for the most part in elderly subjects, it has been seen also in quite young children and in adults of almost all ages.

6. Auricular Fibrillation.—This is a condition in which the normal and coördinate systole of the auricle is also lost. The wall stands in a position of diastole and fine or coarse tremulous movements are seen over the whole of its surface. As has recently been shown it depends upon a wave circulating rapidly through a ring of auricular tissue. Thus it is fundamentally like flutter, but differs from the last in the greater rapidity of the circus movement, and by irregularity and variation of the path followed. The circus movement being irregular, the impulses derived from it and travelling to the ventricle are irregular; they also rapidly succeed each other. The movements of the ventricle are therefore rapid and grossly arrhythmic, and the irregularity is so complete that the condition has been erroneously referred to as *delirium cordis*.

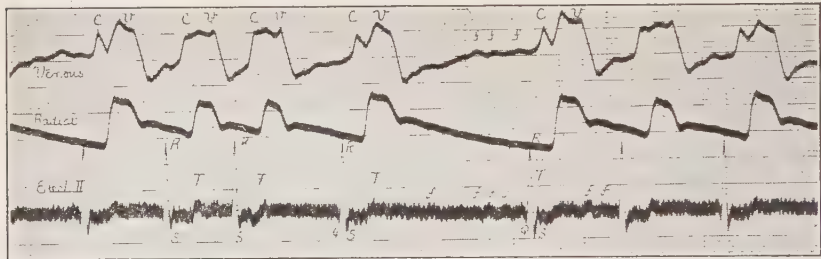
The auricles are readily caused to fibrillate in experiment by faradization; they sometimes pass into fibrillation at stimulation of one or other vagus; the condition also occurs spontaneously in the heart under experimental conditions. With the exception of the faradic current, no certain means of producing it is known. The manner in which circus movements become established in the human auricle is unknown.

Fibrillation of the auricles (Fig. 24) is one of the commonest disturbances of the human heart; it also occurs as a rare event in the horse and dog. In the human subject it is usually a sequel of rheumatic fever or chorea, or occurs in those who have mitral stenosis (about 50 per cent. of all cases of fibrillation). These cases form the largest or "rheumatic" group (70 per cent.), and the heaviest age incidence is between the twentieth and fortieth year. Fibrillation is also seen in senile affections of the heart, and especially between the ages of fifty and seventy years. It is not uncommon in heart disease in renal cases; it is much less commonly associated with aortic disease. Fibrillation of the auricles is essentially chronic, once established it persists for the rest of life, but a small proportion of the patients exhibit it in a paroxysmal form, the attacks lasting a few hours or a few days. Fibrillation is occasionally encountered during the course of acute infectious diseases (rheumatic fever, pneumonia, diphtheria, and pus infections). It is especially frequent in association with Graves' disease. The rate of the ventricle is extremely variable, according to the facility with which impulses pass to it from the auricle; usually between 110 and 150, the complete range of rate is 30 to 200.

The morbid anatomy is not distinctive; as a rule disseminated fibrosis and leukocytosis are found, the auricular tissues being the hardest hit and especially those regions which contain the highly differentiated tissues (the nodes and bundle); but hearts have been described in which these lesions were not found, and the same appearances have been seen where the mechanism was normal before death.

The Effect of Paroxysms of Fast Heart Action and Fibrillation upon the Circulation.—Simple paroxysms of tachycardia and paroxysms of flutter or fibrillation have similar effects upon the circulation. When the heart commences to beat more rapidly it decreases in size; the arterial and venous pressures move in reverse directions and the actual direction is governed by the arterial rate. Where the acceleration is great the arterial pressure falls considerably while the venous pressure rises; but with lesser degrees of acceleration the arterial pressures may remain steady or may actually rise a little. These are the immediate changes

FIG. 24



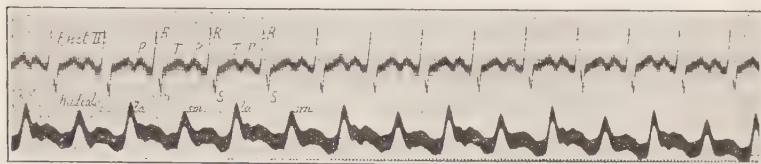
Simultaneous curves in auricular fibrillation. $\times \frac{2}{3}$. The radial curve is extremely irregular, the beats vary both in their incidence and their force. Each pulse beat has a corresponding elevation in the venous curve and this is of the plateau type. In the venous curve there is no *a* wave, whence it is called the "ventricular form of venous pulse," but in the long diastoles very fine oscillations appear; these are due to the fibrillating auricle. Similarly, in the electrocardiogram, the *P* summits are absent and are replaced by rapid and irregular oscillations, marked *ff*; these are derived from the fibrillating auricle and each coarse oscillation corresponds to the completion of a circus movement.

when the heart muscle is tolerably healthy. But in long-continued paroxysms, especially where the reserve power of the ventricular muscle is imperfect, the heart dilates, the fall of pressure is more profound and the blood stagnates in the heart and venous system. Fibrillation of the auricles, and simple paroxysms to a lesser extent, bring forth signs of cardiac failure, in the form of venous and liver engorgement and dropsy, when the heart is unable to accommodate itself to the increased burden which these disorders impose upon it. They do so chiefly by increasing ventricular rate; fibrillation affects the circulation in a minor degree by abolishing the mechanical function of the auricles; these chambers act as reservoirs, taking up the inflowing blood while the systole of the ventricles closes the circulation; in fibrillation the auricular contents are no longer emptied into the ventricles in diastole. This virtual paralysis of the auricles, with the accompanying stagnation of blood in them, predisposes to clotting in these chambers, especially in the appendices. Should

they beat again coördinately the clots may be detached and embolism follows.

7. Alternation.—Alternation of the heart is a condition in which, while the ventricles beat regularly, a large or small quantity of blood is thrown into the systemic circulation at alternate strokes of the pump; or in which the ventricles show alternate strong and weak beats (Fig. 25). It is manifested by hearts which are in a peculiarly weak condition, or, as it is termed, hypodynamic state, or by relatively healthy hearts which are heavily overtaxed.

FIG. 25



Simultaneous electrocardiographic and radial pulse curve, from a case of alternation of the heart. The alternation is clearly seen in the radial curve, a large (*la*) and a small (*sm*) beat succeeding each other alternately. It should be noted that the length of the large cycle is rather greater than the length of the small cycle. No alternation is visible in the electrocardiogram in this, as in most instances.

Thus alternation is seen in experiment when the heart is severely poisoned with such drugs as aconitine, or by the products of asphyxia. Manifested by a ventricle which is not excessively burdened it is a sign of a dying muscle.

Alternation is met with clinically under a variety of circumstances. As a reaction to increased rate, it is seen in paroxysms of rapid tachycardia. When the heart rate is normal, it is often an accompaniment of advanced fibrosis of the ventricles or coronary disease. It is most frequent in the senile heart, in heart and renal disease combined, especially if arterial tension is raised or angina pectoris is prominent. When the heart is disposed to alternate, the occurrence of slight acceleration may disclose it; the occurrence of isolated extrasystoles has a similar effect.

Special Symptomatology.—Sinus arrhythmias and the lesser grades of partial heart-block have no special symptomatology; these disturbances pass unnoticed by the patient. Similarly, in alternation of the heart, though symptoms are usually present, they are associations simply, and are not produced by the abnormal heart action.

Cardiac and Vascular Syncope.—Cardiac syncope is a term which should, properly speaking, be confined to such attacks of loss of consciousness as come from deficiency in the action of the heart as a pump. It is to be differentiated from syncope arising out of vascular disturbances. If a hutch rabbit is held for a period by the ears, its blood accumulates in the splanchnic area and the rabbit loses consciousness owing to failure of the venous return to the heart. A similar phenomenon, sometimes leading to temporary loss of consciousness, or at the least to giddiness, is experienced by many people on passing from the sitting or stooping to the erect

posture. The common fainting attacks of young women have been shown to be due to a vasomotor disturbance, the blood-pressure falling away; presumably there is a dilation of the splanchnic vessels. This disturbance is often associated, though not necessarily, with a vagal slowing of the heart to 40 or 50 beats per minute. Similar attacks, from which recovery is invariable, occur in young men, and they are also quite common in the subjects of heart disease (including aortic regurgitation); in fact the attack of this kind is by far the commonest type of syncope experienced by cardiac patients. All these subjects are particularly prone to the attacks while in the erect posture, and the assumption of the horizontal position brings relief. The vaso-vagal seizure is usually accompanied by pallor, sweating and often by nausea, sometimes by vomiting. Cardiac syncope, properly so-called, is much rarer than the varieties of syncope just described. In both the vascular and cardiac forms, loss of consciousness is due to anemia of the brain, but whereas in *vascular syncope* the supply of venous blood to the heart is deficient, in *cardiac syncope* this is not the case; in this the heart is at fault and fails to transfer the plentiful venous blood supplied to it to the systemic arteries. If the arteries to the head are compressed (in man compression of the carotids suffices), the face blanches and in a few seconds the subject becomes giddy and a little later loses consciousness (Kussmaul and Tenner). More prolonged compression results in deep sighing respiration and convulsions. The same phenomena are seen in profuse hemorrhage.

If the venous return to the ventricle fails or if the ventricle refuses to throw blood into the arterial system, precisely the same symptoms follow; thus, if the ventricle ceases to beat for from three to seven seconds, or if the rate falls to 8 to 20 beats per minute, unconsciousness results. After asystole of some fifteen or twenty seconds' duration, the veins become distended and cyanosis, stertorous respiration, and a twitching of the face and upper limbs are added to the symptoms. The heart fails to transfer the incoming blood from the venous to the arterial side (1) when the ventricles cease beating (true asystole), and (2) when the ventricles beat very rapidly. The varieties of cardiac syncope are as follows:

1. *Ventricular asystole* which happens in one of three known ways:

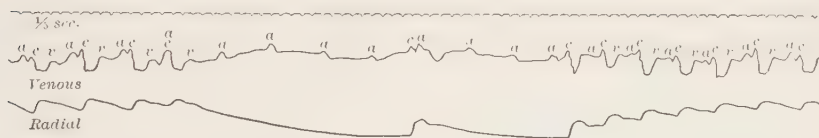
- (a) In rare cases in which there is a disturbance of impulse production (see page 393). The whole heart beat is suspended in this condition, which is probably of vagal origin in most instances.

- (b) In cases of heart-block. In those patients who suffer from high grades of partial heart-block or in those in whom complete dissociation is present, attacks of giddiness, of momentary loss of consciousness, of longer unconsciousness with cyanosis and epileptic manifestations are very common. In the fits the ventricular action is extremely slow or ceases for shorter or longer periods; the auricles continue to beat. The severity of the attack is conditioned by the degree of slowing or by the length of time over which the ventricular beats lapse. Death results when the ventricular asystole is of from one to two minutes' duration. In heart-block the attacks may be absent or infrequent, occurring at intervals of many months or years. In other patients they are more frequent, coming weekly or daily, or occurring successively over periods

of several hours or several days and producing a picture not unlike the *status epilepticus*. As a rule the patient has no warning of an impending fit; though on occasion a preliminary pulse slowing or momentary periods of giddiness may serve as signs of the approaching danger; the sensations at the commencement of long seizures are similar to those accompanying a brief cessation of heart beat and do not properly constitute an aura. Incontinence of urine and tongue-biting are extremely rare, and a knowledge of this fact aids diagnosis; the petechial hemorrhages which occur in true epilepsy are not found. If the patient is seen in the attack its nature is recognized by the slow ventricular action and by the signs of the auricular contractions which are visible in the veins of the neck.

The fits of partial heart-block are the result of temporary increase in the degree of block. Repeated cardiac syncope is also seen as an infrequent manifestation in temporary and recurring attacks of heart-block (Fig. 26). The period during which partial is developing into complete block is one of special danger to the patient. In some cases the increase of heart-block seems to have been of vagal origin and atropine has given relief. The cause of the ventricular standstill in most cases of complete heart-block is unknown; it is of interest to note that exactly comparable attacks were witnessed by Erlanger in his experiments upon dogs.

FIG. 26



Venous and radial curves from a patient who suffered from numerous and short attacks of cardiac syncope. $\times \frac{1}{2}$. The curves show the nature of the attacks. The ventricular contraction ceases first for five seconds, then for three seconds; the whole period of disturbance being associated with a loss of consciousness. The normal heart action is then resumed. During the period of ventricular slowing, the auricle continues to beat at its former rate. The syncopal attacks were due to the sudden onset of temporary heart-block.

(c) Asystole may be the result of *fibrillation of the ventricle*. As a cause of convulsions in the human subject it is extremely rare; as a cause of sudden death it is probably common, and from this standpoint it will be described and will receive further consideration at a later stage (see page 421).

2. *Rapid Action of the Ventricles*.—Loss of consciousness may be produced by extremely rapid action of the ventricles, rates of 200 per minute and more. With great acceleration of the ventricles, or with lesser acceleration when the circulation is failing, little or no blood is forced into the arteries; the blood-pressure falls toward zero and consciousness is lost. The attacks to which the subjects of auricular flutter are prone are due to this cause. As a rule the ventricular action is much slower than the auricular in this condition, but occasionally the ventricle beats at the same rate as the auricle, and the acceleration may be as much as even 290 or 300 per minute; in these circumstances consciousness is usually lost.

Stokes-Adams syndrome is a term which has been applied to attacks of syncope or convulsions associated with habitually slow pulse action. As a rule the association is due to the presence of heart-block; but slow action of the ventricle may result from slow action of the whole heart, and this may be combined with similar attacks or with momentary seizures of extracardiac origin. Several cases are on record also in which in true epileptics the *pulse* was slow for long periods, because extrasystoles were present. These variations in the clinical picture and the diverse causes of syncope generally, emphasize the need of detailed study of the individual case whenever the nature of convulsions is not abundantly clear.

The Symptoms of Premature Beats.—In a large number of affected patients the abnormal beats pass unperceived. On the other hand these premature beats constitute one cause of what patients term "*palpitation*." The symptom is more prominent in the young and especially in those of female sex and in those of nervous temperament. The intermittence awakens a feeling of uneasiness or oppression in the chest, or a feeling of void, while the succeeding contraction is accompanied by consciousness of shock to the chest wall and often by a feeling of gripping in the throat. By calling attention to the heart they induce anxiety. The sensations are exaggerated by general depression of the health, by fatigue and by emotion. They are often more noticeable at night, after excessive smoking, after a heavy meal, or after exertion. When numerous they may occasion actual distress, especially if they are grouped together; anxiety may be profound under these circumstances and faintness, coldness of the extremities and sweating may result.

The Symptoms of Paroxysmal Tachycardia.—The symptoms in simple paroxysmal tachycardia, in paroxysms of flutter and in paroxysms of fibrillation are alike. In a given patient the length of the paroxysms is fairly constant; in some they are infrequent and of long duration; in others they are frequent and of short duration. The symptoms are controlled by the length of the paroxysm, by the rate of the heart beat during them, by the state of the heart muscle, and by the reaction of the nervous system; they are consequently very variable. In short and relatively slow paroxysms there may be no symptoms and in longer and more rapid attacks they may be severe.

The immediate onset is signalled by discomfort in the region of the heart, which may amount to slight or violent palpitation. A sense of tremor or fluttering in the chest, a beating in the neck, is common. Lassitude, exhaustion, coldness and sweating are early symptoms. Later, flatulence, nausea and vomiting may be prominent. The alimentary symptoms, once established, persist till the attack is over; they hasten the exhaustion which is conspicuous in attacks of long duration. In some patients anginal symptoms are added, varying in intensity from soreness of the chest and a sense of compression, to violent and radiating pains. Symptoms and signs of cardiac embarrassment are often seen and increase as the attack proceeds. The limits of dulness and the orthodiagraphic outline, at first diminished, increase progressively during the course of the attack. To pallor, which is often conspicuous

at an early stage, cyanosis is added, the eyes seem sunken and dark areas appear around them. The veins and liver swell gradually, and tenderness and pulsation are found over the last-named organ. Aching pain develops in the epigastrium and hypochondrium. A cough, accompanied by frothy and at last blood-stained expectoration, develops with signs of bronchitis or congestion and œdema at the bases of the lungs. Collapse is prominent in the later stages; the attack may terminate in progressive failure, delirium, ascites, general anasarca and death. Unexpected death terminates the paroxysm on occasion, but in most instances there is an abrupt recovery and this may come at any moment. The cessation is marked by symptoms of its own, a sharp, stabbing pain, one or more forcible shocks of the heart. Usually the patient speaks only of relief. The rapidity with which the symptoms and signs vanish is remarkable. The dilated veins and heart contract in size, the liver recedes less rapidly below the ribs. Quantities of flatus are expelled and limpid urine is often voided after an attack. For several days there may be a sense of exhaustion and soreness of the chest.

Stasis in the lungs during paroxysms, with dulness and crepitations at the bases, has been mistaken for pneumonia. Severe abdominal pain, anginal or hepatic, with conspicuous collapse and running pulse have been mistaken for perforated gastric ulcer. A large number of the cases have been carelessly grouped as instances of "acute dilatation" or "heart strain," especially when paroxysms have succeeded unwonted efforts or when they occur in the pregnant woman (see remarks on dilatation and tachycardia, page 391). Forcible beating in the veins of the neck, with a distention of the jugular bulb on the right side may closely simulate innominate aneurism.

Symptoms in Continued Flutter and Fibrillation of the Auricle.—In patients in whom auricular flutter or fibrillation is continuous, the symptoms vary, as in paroxysmal tachycardia, according to the rate of the ventricular action and the state of the heart muscle. In many patients they create little disturbance, in these the ventricular action is slow and the muscle relatively strong. In others dilatation of the heart, engorgement of the veins, cyanosis, enlargement of the liver and dropsy appear and persist. These are cases in which the rate is rapid and the muscle fails to meet the added burden.

Thus the symptoms are largely those of a degenerate and failing heart muscle, symptoms which may come in the absence of flutter and in the absence of fibrillation. They are promoted by rises of ventricular rate when the muscle is already fully taxed; and therefore, frequently appear when flutter or fibrillation appears, persisting so long as the increased rate is maintained. If the muscle is less degenerate, or, what amounts to the same thing, if it is less heavily burdened beforehand, the appearance of these disorders may give rise to no serious circulatory embarrassment. The importance of flutter and fibrillation from the clinical standpoint lies in the rate which they engender in the ventricle. A degenerate muscle is unable to tolerate the strain of greatly enhanced rate.

Clinical Distinction of Cardiac Irregularities.—Preliminary Evidences.—*Incidence.*—In hospital practice auricular fibrillation is responsible for the largest number of irregular hearts; premature contractions are almost as frequent; the remaining disorders are much less frequent.

Age and Frequency.—Irregularity in young children is almost always of sinus origin; premature beats and heart-block have been described but are rare in early years; fibrillation of the auricles is almost unknown before the age of thirteen, and is extremely rare before the seventeenth year; flutter is rare in children.

Heart-rate.—*When the ventricle is regular* in its action and its rate is below 35 per minute, complete heart-block is usually present (Fig. 4); a rate of 40 to 50 suggests but by no means proves partial heart-block. A persistent heart-rate of 130 and over should always bring a long-continued paroxysm of tachycardia to mind. *If the ventricle beats irregularly* and the rate surpasses 120, fibrillation is generally present; and as the rate is faster so the diagnosis becomes more certain. Premature contractions are rarely seen at heart-rates of 120 and over; sinus arrhythmias are almost confined to rates below 100.

Persistence of Irregularity.—Auricular fibrillation is the only disorder in which the action of the ventricle is permanently irregular. All other irregularities are transient, or broken into from time to time by periods of regular action.

Common Clinical Types and their Meaning.—Intermittence of the Pulse.—An occasional long pause in an otherwise regular pulse is due to one of two causes; namely, a premature contraction which fails to affect the arteries, or a failure of the ventricle to respond to an auricular contraction (heart-block).

Coupled Beating and Triple Beating (Bigeminy and Trigeminy).—These phenomena are due similarly to premature beats (Fig. 20) occurring at regular and frequent intervals or to heart-block (Fig. 18), frequent ventricular responses being missed at regular intervals. *Halved pulse rate* may be due to halved ventricular rate or to premature beats replacing each second normal beat and themselves failing to reach the pulse.

Halved Ventricular Rate.—A sudden and exact halving of ventricular rate is always due to heart-block.

Regular tachycardia may result from simple acceleration, simple paroxysms of tachycardia or auricular flutter.

Irregular tachycardia and gross irregularity of the ventricle, both in the rhythm and force of its contractions, are almost always the result of auricular fibrillation; exceptionally they may be due to frequent premature contractions or to heart-block, especially when the latter is associated with flutter.

While different forms of disordered action may usually be recognized by simple bed-side tests, the absolute diagnosis of a particular disorder is made by the employment of graphic records. By polygraphic or electrocardiographic means, the relative positions of the contractions in auricles and ventricles may be identified and compared. Those who desire full information and descriptions of these methods should refer to special treatises dealing with them. The signs by which the chief forms

of altered heart action may be identified are set forth in the following paragraphs:

Recognition of the Disorders.—*Simple Tachycardia.*—When the ventricular rate is raised and the enhanced action is a simple acceleration of the whole heart:

(a) The rate is greater after exercise, with emotional disturbances, in the erect posture, and after the administration of such drugs as amyl nitrite or atropine.

(b) It falls considerably during the first few hours or days after the patient takes to bed; it falls by 10, 20, or 30 beats per minute when the erect posture gives place to a horizontal one.

(c) The rate is rarely over 140 while the patient rests in bed.

(d) The rise of rate is gradual, its fall is equally gradual, the rate varies considerably from time to time.

(e) There is as a rule no reaction to digitalis.

(f) Electrocardiograms are of normal outline (see Fig. 16).

Simple Paroxysmal Tachycardia.—This form of acceleration is recognized in the following manner.

(a) The rate is almost constant with exercise and under emotional changes.

(b) It varies little, if at all, with posture.

(c) The ventricular rate often exceeds 140, and may remain at 200 per minute even after the patient has reclined for hours or days.

(d) The onset of the tachycardia is abrupt; its offset is equally abrupt.

(e) It rarely lasts more than ten days; it may last but a few seconds.

(f) Digitalis produces no slowing and no irregularity.

(g) The electrocardiograms show an equal rate of auricle and ventricle, and an abnormality in the seat of production of the beats. These may arise in the ventricle or in an ectopic auricular focus (Figs. 20 and 21).

Auricular flutter usually occurs in elderly subjects. When the ratio of contraction of auricles and ventricles is as two to one:

(a) The ventricle beats regularly at rates varying between 100 and 170.

(b) In a given case the ventricular rate is constant under a variety of circumstances, as in simple paroxysms.

(c) The onset and offset are not often witnessed, but are spoken of as abrupt. The duration is usually several months or years.

(d) Digitalis always produces slowing and irregularity.

(e) Pressure upon the carotid sheath and vagus has similar results.

(f) In the veins of the neck, extremely rapid undulatory movements are sometimes to be seen and may be recorded (Fig. 23).

(g) Electrocardiography shows two auricular contractions to one ventricular and an auricular rate of from 200 to 340 per minute (Fig. 23).

When the ratio between auricular and ventricular contractions is greater, the diagnosis is more difficult, but:

(a) The rapid undulations in the jugular vein are then more often conspicuous.

(b) Occasionally the rapid auricular contractions can be heard with the stethoscope.

(c) If the pulse is regular at 70 or 80 per minute, it will rise abruptly to exactly double this rate with exercise.

(d) If the pulse is irregular, the beats are curiously grouped and the same phase of irregularity is frequently repeated. It becomes regular and more rapid with exertion or atropine.

(e) Electrocardiograms will always identify the rapid auricular movements.

Sinus irregularity is easily recognized:

(a) It is specially prominent in children.

(b) The rise and fall of pulse rate is periodic and accompanies the natural or deepened acts of breathing.

(c) A rise of heart rate, from whatever cause, gradually abolishes the irregularity, which is very unstable.

(d) Polygraphic and electrocardiographic curves show the auricle and ventricle to participate equally in the irregularity. The electrocardiograph demonstrates that each heart beat arises normally (Fig. 17).

Simple Bradycardia.—In simple bradycardia:

(a) The ventricular rate is rarely less than 50 per minute.

(b) Pulse and ventricle beat at the same rate; the rate rises with exercise, atropine or amyl nitrite, and falls again subsequently.

(c) The movements of the veins are synchronous with the several heart beats. Polygraphic curves show auricular and ventricular waves in their normal sequence.

(d) The electrocardiograms are normal except that the groups of deflections are widely separated.

Partial Heart-block.—In this condition:

(a) The heart's action is intermittent, grouped, or regular and slow.

(b) The rate of ventricle and pulse is the same and the irregularity is parallel in both.

(c) The ventricular rate often lies between 40 and 50 per minute.

(d) All irregularity is abolished by exercise and usually by atropine.

(e) Abrupt changes of ventricular rate to a half or double the former rate are apt to occur.

(f) In polygraphic and electrocardiographic curves the auricular contractions are more numerous than the ventricular ones (Fig. 18).

Complete Heart-block.—Where dissociation exists:

(a) The ventricular rate has usually fallen to 30 per minute or thereabout. The ventricle beats regularly and its rate is uninfluenced by exercise, atropine or amyl nitrite.

(b) Attacks of giddiness or loss of consciousness are usually to be found in the past history.

(c) Auricular waves may be seen in the veins of the neck, occurring during the long diastoles. The venous pulsation often waxes and wanes independently of respiration. The auricles may be seen to beat more rapidly than the ventricles on the fluorescent screen.

(d) The heart sounds are peculiar; a first and second sound is heard with each ventricular systole, but these sounds vary in intensity in an extraordinary manner or show varying reduplications from cycle to cycle. The auricular sound, very distant and muffled, may often be heard over the auricles or at the apex beat or epigastrium.

(e) In polygraphic and electrocardiographic curves, the auricular and ventricular movements are regular but at distinct rates, the auricular rates are those of the normal heart beat or somewhat in excess of it. Auricular and ventricular contractions frequently coincide (Fig. 19).

(f) Very frequently minute auricular waves may be seen upon arterial curves (Fig. 19).

Premature contractions are easily recognized because:

(a) They are responsible for intermittence of the pulse and for most instances of grouped action of ventricle and pulse.

(b) The rate of ventricle and pulse is often different. Many of the premature beats fail to affect the pulse. When the pulse is intermittent, single premature beats are palpable or audible at the apex beat. The ventricular rate may be double the pulse rate. If the pulse beats in paired fashion, the ventricle often beats in groups of threes.

(c) The heart sounds are often peculiar. Those premature beats which fail to reach the wrist are accompanied by first sounds only and these are premature sounds. The heart sounds (first and second) are heard in groups of three or four sounds when the pulse beats are coupled.

(d) Premature beats are abolished by rises of heart rate.

(e) They are readily identified in polygraphic curves, and are seen to come, some from the auricle, some from the ventricle (Figs. 20 and 21).

(f) In electrocardiograms the pictures are even more characteristic. These beats arise in abnormal foci; the contractions run along abnormal paths in one or other heart chamber and often give rise to highly abnormal pictures (Figs. 5 and 6).

Auricular fibrillation is distinguished as follows:

(a) The most reliable clinical test is based on the association of irregular and rapid action of the ventricle. If the heart beats irregularly and the ventricular rate is 120 or over, fibrillation is usually present; the higher the rate in these circumstances the more definite becomes the diagnosis. Irregularity with a ventricular rate of 170 and over is unknown apart from fibrillation. If the ventricular action is relatively low, it may be raised by exercise, by atropine or by amyl nitrite; the same conclusions may be drawn when the heart remains irregular while beating rapidly in these circumstances, as when the rapid beating is spontaneous. Thus, if a patient whose heart is irregular at a rate of 100 is exercised mildly, the rate will usually rise. It will rise with particular ease in fibrillation, and the heart remains irregular while for a period it beats at 140, 160 or 180. The last rate is decisive, the first two are practically so, in the presence of irregularity.

(b) If the patient is instructed to take deep breaths, the pulse sometimes quickens in inspiration, sometimes in expiration.

(c) The irregularity is persistent.

(d) It is often associated with signs of heart failure, and occurs in young adults and elderly people.

(e) The pulse and ventricular action are often grossly irregular (Fig. 24). The type of irregularity and its degree are however very variable, and the recognition of fibrillation from the character of the irregularity, ascertained with the unaided senses, is often precarious. For this reason this feature is placed fifth on the list.

(f) The ventricular rate when raised is conspicuously affected by adequate doses of digitalis.

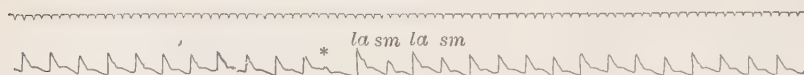
(g) In cases of mitral stenosis, with which it is commonly associated, an isolated presystolic murmur is not heard; and if the ventricular rate is slow this murmur is replaced by an early diastolic murmur.

(h) In polygraphic curves the "ventricular form of venous pulse" is found, that is to say, there is no sign of a presystolic wave resulting from auricular contraction. The fibrillating auricle may give rise to fine oscillations on the curve in long diastoles (Fig. 24).

(i) The electrocardiograms show no sign of coördinate auricular contractions. The normal auricular summits are replaced by characteristic oscillations which run throughout the whole curve and are especially prominent in diastole (Fig. 9).

Alternation of the Heart.—This condition is occasionally recognized in estimating systolic blood-pressure; alternate beats force their way through the armlet at higher pressures. Usually it is found only when deliberately sought in arterial curves (Fig. 25). It is wise to examine with the sphygmograph cases of angina pectoris, all cases of high blood-pressure and all elderly subjects in whom affections of the heart are suspected, or in whom renal disease is known to exist, with the specific object of determining the presence or absence of alternation of the pulse. It should be sought also after premature beats (Fig. 27) in all elderly subjects and in all cases of heart disease.

FIG. 27



An arterial curve showing the appearance of alternation of the pulse for two short periods after the occurrence of a single extrasystole. $\times \frac{1}{2}$. The extrasystole is marked with an asterisk.

Prognosis.—In dealing with cardiac patients, prognosis occupies a prominent place. We are asked to foresee the probable duration of life under given circumstances; we are expected to foretell the measure in which our patients will suffer from subjective disturbances and if and when these will subside. Lastly, we have to determine the possibility or probability of sudden and unexpected death. We are asked much; with careful study and deliberation we can prophesy a little.

The forecast in patients who complain of cardiac symptoms is based upon a number of considerations.

1. Our first duty is to ascertain, where this is possible, if disease of the heart is the primary fault and carefully to exclude such disturbances of the circulation as are the result of defects in other organs.

2. If it is in the heart itself that the primary weakness is discovered, or if the heart has been seriously and permanently damaged by coexisting disease in other organs, we must first attempt an estimate of the strain which the organ has to bear. It may be that the heart works at a disadvantage, that it has to force the blood through a constricted orifice,

or that it is unable to choose its own and suitable rate of beating. The burden may be smaller than, equal to, or greater than, normal.

3. We should endeavor to arrive at an idea of the functional efficiency of the muscle, and especially that of the ventricle, considering particularly the degree of reserve, its plenitude or its limitation. And we should consider the efficiency from the standpoint of the work to be accomplished and the circumstances under which this work is undertaken.

4. We must ascertain, where we can, the probability of change in the relations between work and efficiency for work in the near future. Is the disease stationary or progressive? Will the efficiency increase with appropriate treatment? In respect to the latter, it may be wise to delay a full statement until the effects of such treatment are seen or the course of the malady under treatment begins to be evident.

5. Lastly, we must be fully acquainted with the progress of symptoms in the several disorders and have particular knowledge of those in which sudden catastrophies occur at all commonly.

Prognosis in any given case takes us therefore over a wide field. Our present purpose is to inquire whether we are aided by recent observations upon disorder of the heart's action; and if so, in what direction and to what extent? We shall find they aid us materially and in many directions.

It is essential to recognize that prognosis in heart affections cannot be based upon what we regard as the probable macroscopic and microscopic lesions. Prognosis upon a purely anatomical basis is insufficient; speaking generally, at the present time the reason of death is not revealed by the dead organ. While anatomical and mechanical reasoning has occupied the foreground of the argument, this argument has been incomplete. Observation of the heart as a living and moving organ; study of its movements, be they normal or perverted, by exact methods; observation of the reaction of the heart to altered conditions, form the readiest paths to the desired information.

Tachycardia.—To discriminate between the varieties of tachycardia is the first essential. The heart rate may be raised, its action may be regular or irregular. At present we may consider the former. As we have seen, regular tachycardia is of three varieties; they have been termed simple tachycardia, simple paroxysmal tachycardia, and auricular flutter. The prognosis, like the treatment, is different in the three states.

Simple Tachycardia.—Having determined the presence of a simple tachycardia, attention should no longer centre upon the heart. The rapidly beating organ is but an indicator, telling of a disturbance of innervation or of an altered physical or chemical environment. The discovery of an enlarged thyroid, signs of intoxication, a focus of infection or instability of the nervous system, reveals the cause of the acceleration and guides prognosis. It should not be forgotten that simple acceleration may accompany disease of the heart itself, and this has to be taken into account in the prognosis of mitral stenosis and of aortic disease.

Simple paroxysmal tachycardia should for the present be regarded as primarily a cardiac condition. The prognosis of the individual attacks contains an element of uncertainty. Death during paroxysms is not very infrequent in the affected, but considering the attacks themselves,

this termination is rare. The severity of the symptoms is influenced largely by the reaction of the nervous system; neurotic people awaken undue anxiety. The duration of the observed paroxysm and the length of previous paroxysms have to be considered; the duration is fairly constant in a given case; the paroxysms generally terminate before a week or ten days have passed, usually they last a few hours. They are not commonly terminated by treatment. The outlook is more ominous when after several days, the heart still shows signs of progressive failure and when œdema of the lungs, delirium and dropsy appear. Nevertheless it often happens that at the height of the embarrassment the paroxysm ends and relief is immediately obtained.

The prognosis of the malady as a whole is based upon an estimate of the endurance of the cardiac muscle between the attacks and upon the severity of the attacks. The first prognostic evidences are the same as in a similar case where there are no attacks, with the following reservations. The attacks are themselves indications of muscle damage and they may jeopardize the life of the patient. The reaction of the heart to the attack is important. A healthy heart reacts to increase of rate by decreasing in size, and if the acceleration is not extreme, the circulation may be maintained for long periods. A diseased ventricle reacts after a short while by dilating. The degree of dilatation, the rapidity of its onset and progress suggest the degree of muscular involvement. Secondly, the severity of the attacks in respect of duration, frequency, and rate of the heart's action is summed up; but as the attacks may cease at any time, never to return; and as we do not know to what extent paroxysms damage the heart, if they damage it at all,¹ the value of these considerations in completing the prognosis is limited. The possibility of unforeseen death in a paroxysm necessitates some, but not undue, caution in prognosis.

Patients inquire as to the prospect of the attacks ceasing; in young subjects, if the heart is sound while it beats normally, they may be told that, while freedom cannot be promised, the prospect of it is fair.

Auricular Flutter.—When flutter develops, it throws an increased strain on the heart, proportioned to the increase of ventricular rate. Untreated it is usually a persistent condition. If the muscle is degenerated and the rate rapid, signs of failure supervene and if unrelieved the patient's condition is precarious. On the other hand, when it occurs in a tolerably healthy heart, much circulatory embarrassment is unusual. The influence upon the life history in these circumstances is not fully known; though its persistence for eight years has been recorded, the ventricle beating continuously at 150 per minute, or more. It is a condition which often reacts in splendid fashion to treatment; the forecast is more readily accomplished after this has been undertaken. If it is abolished by treatment, it may or may not return, but in the last event further treatment is often successful.

¹ The question of strain and its effect upon the heart has long been the subject of controversy; of all the strains to which the heart is submitted none are so severe or of such long duration as some of these paroxysms, yet they seem to leave no aftermath.

Auricular Fibrillation.—As in other kinds of arhythmias, the prognosis is governed largely, if not chiefly, by the remaining signs, and especially by an estimate of the strength and reserve of the muscle, and by the size of the heart. But fibrillation is itself a sign of muscle involvement; occurring in acute illnesses it indicates invasion of the myocardium; as a chronic condition it is generally associated with disseminated and chronic inflammatory lesions, leading up to diffuse fibrosis. Fibrillation of the auricles loads an already defective muscle with an extra burden, the burden of increased ventricular rate and shortened diastole. It heralds cardiac failure, temporary or permanent; very few patients survive its onset for more than ten years; as a rule the end comes more speedily; however, in one case it has been known to persist for thirty years. The degree in which the acceleration may be controlled by appropriate remedies, forms a chief prognostic consideration.

In a given patient, the prognosis becomes very distinctly less favorable when fibrillation develops. Yet if two untreated patients show an equal grade of cardiac failure and one presents fibrillation while the other does not, the prognosis is more favorable in the former; for fibrillation imposes a burden upon the heart and, as it is particularly amenable to treatment, this burden may be in large part removed. The difference in the condition of the two patients considered, when they come under treatment, is often conspicuous; the patient presenting fibrillation reacts well, the other frequently does not do so. The prognosis in paroxysmal fibrillation is similar to that in simple paroxysmal tachycardia, with the reservation that such patients more frequently develop permanent fibrillation than do the subjects of the simple attacks.

Slow Action of the Ventricle and Heart-block.—*Simple Bradycardia.*—As in the case of simple tachycardia, the prognostic significance of slow action depends upon the cause, and this is usually extracardiac when the rate lies between 50 and 70. It is probable that where the pulse-rate lies between 30 and 45, the cause is as a rule intracardiac; yet such patients progress favorably, providing that signs of muscle efficiency are present. Of the relation of *vagal standstill* to the life history we have incomplete knowledge. The patients may show complete recovery. Death as a result of vagal inhibition of the heart's action has not been proved, neither has its existence been shown to be probable; where the muscle seems healthy, and no gross disease affecting the vagi can be identified, the patient should be reassured.

Heart-block.—Those who die exhibiting heart-block usually die with signs of general heart failure. It will be understood that heart-block and the Adams-Stokes syndrome are by no means synonymous terms and that most subjects of heart-block never have convulsions; the lesser grades of heart-block are by far the commonest and are frequently associated with rheumatic heart disease. Where partial heart-block is persistent there are usually other signs of cardiac involvement; the presence of heart-block gives an added significance to the case. It is an evidence of myocardial damage, not necessarily limited to the conducting tract, but usually disseminated throughout the more silent areas of the muscle.

Partial block which is temporary is often associated with acute infectious disease, as in rheumatic fever and pneumonia. Occurring in these conditions it is a sign of the gravity of the infection; it may be the sole indication that the myocardium has been damaged. Occurring in patients who suffer from rheumatic heart disease, it is to be regarded as an outward sign of an isolated injury which, if repeated, eventually so weakens the muscle that life is no longer supported.

In the higher grades of block, in addition to the general evidence of integrity of the muscle or the reverse, the convulsions have to be taken into account. Some patients are free from them, in others they are frequent and severe. Those patients in whom the lesions are progressive and in whom partial is passing to complete block, must pass through a time of particular danger, for then convulsions are often frequent. Regarded in its entirety, persistent heart-block of high grade is a grave condition. The bundle defect is usually complicated by other muscle lesions and the mortality is very heavy. The ease with which autopsies have been obtained in these patients speaks for the seriousness of the malady. Nevertheless, some patients survive in comparative or absolute comfort for many years. They are for the most part young subjects, and those in whom the remainder of the heart muscle is comparatively healthy.

Sinus Arrhythmia and Premature Beats.—*Sinus Arrhythmias*, with the exception of standstill of the heart, have little or no prognostic significance. In young subjects these irregularities are to be regarded as normal phenomena; if they are recognized they are not confused with more serious disturbances. Irregularity of the heart has long been regarded as ominous; today we know that certain irregularities are of no consequence in prognosis.

Though *premature beats* are decided evidences of pathological defects in the heart; yet while they are so common in apparently healthy subjects, and while they may persist from early to advanced years, they cannot be said seriously to affect prognosis. The heart is quite healthy in but a few adult subjects living under modern conditions; the significance of slight changes in the muscle must be regarded from the comparative standpoint. The sole reservation in regard to premature contractions applies to their occasional presence as precursors of paroxysms of tachycardia or of permanent auricular fibrillation. In the great majority of those patients in whom they are seen, the more serious disorders will not develop.

Alternation of the Heart.—The gravity of the malady in a patient who exhibits this sign is often borne witness to by the association of angina, nocturnal dyspnoea, Cheyne-Stokes breathing or high blood-pressure. But its special value lies in the fact that while each and all of these symptoms may be absent, alternation may be present and foretell the future. Accompanying a normal or slightly enhanced heart rate it speaks clearly of muscle exhaustion. If continuously present, a favorable prognosis is always forbidden and such a forecast is rarely justified when it appears even temporarily in the pulse. The only propitious circumstances, when it is seen, are a history of exceptional and prolonged

strain, which may be immediately avoided for the future, and evidences of acute intoxication which are disappearing.

Treatment.—Treatment, dictated by the rate and mechanism of the heart's action, is directed by a few clear principles.

1. The nature of the disturbance being recognized, we are often able to decide whether it is the heart which is primarily at fault, or whether a healthy musculature is merely responding to abnormal influences, be they nervous, chemical or physical.¹ Our first endeavor is to locate the mischief, either in the heart or outside it, and to treat our patient accordingly. If the musculature can be declared healthy, the heart is no longer our chief concern. If the heart is itself involved, then:

2. We search for etiological factors, and especially for the source or channel of an infection; we remove the former or seal the latter, and in this fashion we may be successful either in cutting short the whole disturbance or in preventing or retarding its progress. In rare instances we may treat an infection by specific measures.

3. In the cases of periodic disturbances, we guard against the provocative causes of such crises.

4. When the disturbance is an established one, we may at times employ such remedies as abort it; more frequently treatment will resolve itself into:

5. Adjusting a proper relation between the work which the heart has to do, and its capacity for such work; and thereby prolonging the life of the subject. There remain:

6. Remedies employed for the relief of symptoms.

7. Precautionary measures for the avoidance of sudden catastrophes.

Simple Tachycardia.—The treatment of simple tachycardia requires little discussion. It is controlled by knowledge of its cause, and the remarks which have been made under diagnosis and prognosis are sufficient guides to treatment which is considered in detail in other chapters of this system.

Simple Paroxysmal Tachycardia.—The treatment resolves itself into that applied during the crisis and the care of the patient during the general course of the malady.

We are aware of no unfailing remedy which will abort the attacks. Some few patients are able to terminate the seizures by assuming a peculiar posture, by taking deep breaths or by inducing vomiting. Deep pressure applied successively on the right and left carotid sheath should be tried; in a number of recorded instances the paroxysms have terminated as a result and the procedure is without danger. The application

¹ Our knowledge of the pathology where there are disorders of sequence is still incomplete; in dealing with simple tachycardia we may assume an extracardiac origin of the disorder in almost all instances; it is not so clear that simple paroxysms of tachycardia or fibrillation or profound slowing may not be of purely nervous origin. Still we require a definite basis for therapeutic measures and today it seems improbable that the named disturbances arise when abnormal nervous impulses play upon the healthy organ; it is more probable that they appear when the heart responds in an abnormal fashion to such impulses. There is an evident overlapping on the chemical side; abnormal nutrition or poisoning may certainly be responsible for both simple sinus disturbances or actual disorders of sequence.

of an ice-bag to the precordium, a remedy which always affords relief, may speedily bring the desired ending. I have seen attacks terminate after single injections of digitalis or strophanthin, but regard these as uncertain remedies. The application and retention of a tight abdominal binder sometimes serves in abolishing numerous attacks each of a few seconds' duration. Usually, radical treatment is of no avail, and the remedies relied upon are palliative. Rest is enjoined, though the wishes of the patient in respect of posture are considered. In severe attacks sudden movement of any kind is forbidden and it is advisable that the patient should be fed by hand and that the bowels should be cleared by simple enemata in paroxysms of long duration. The dietary should be fluid, bland and as restricted as possible. Iced water or milk, albumin-water or beef-tea are suitable. Local applications, the ice-bag, mustard plaster, leeches or cupping, applied over heart or liver, according to the seat of pain, often bring relief. Severe pain may be treated with chloral or morphine; and these remedies may also be used to induce sleep which is often deficient; the encouragement of sleep is always clearly called for. Great engorgement of the heart, or the appearance of engorgement of the lungs or dropsy, suggests venesection. The letting of 8 to 16 ounces of blood will be followed by improvement; but the occasion for it does not often arise. Simple expectorants may be used for the cough. Pure oxygen is administered when there is deep cyanosis.

In treating the malady as a whole, a searching inquiry may reveal exciting causes of the paroxysms, which may be removed; sudden emotion or exertion may be the chief provocative factor, and it may become necessary to interdict active employment. The relief of oral and pharyngeal sepsis, the remedying of dyspeptic troubles, and detailed attention to the general habits of the patient, the moderation or banning of tobacco, alcohol and sexual excitement, are important considerations. Eventually and in long-continued paroxysms, a full course of digitalis may be advisable.

Auricular Flutter.—When paroxysmal the treatment of this condition is similar to that of simple paroxysmal tachycardia. Persistent flutter is treated with drugs of the digitalis group. If the course of the drug administration is carefully supervised by graphic methods, notable successes are often achieved. Digitalis in the form of the tincture or infusion is given in stiff doses: about $\mathfrak{5j}$ (4 cc.) daily of the tincture, $\mathfrak{3iij-vj}$ (12-24 cc.) daily of the infusion, until, as always happens when the ventricular rate is originally rapid, ventricular slowing is obtained. According to the needs of the patient the drug is pushed further until the ventricular rate falls to 70, 60 or 50; the dosage may then be reduced and regulated so that a normal ventricular rate is maintained. But often at the time of profound slowing, the auricles fibrillate and, if the drug is then withdrawn altogether, the normal heart action usually becomes reestablished. I have seen this curious reaction in a number of patients, and it always affords conspicuous relief. The normal rhythm may be maintained indefinitely; in some patients the flutter returns again and requires a repetition of the treatment; in cases which cannot be relieved in this manner, the treatment should be similar to that employed in fibrillation. Quinidine as a remedy

for flutter is not often successful and is scarcely to be advised, since the drug is apt to induce dangerously high ventricular rates. It seems very possible that by combining digitalis and quinidine therapy, each of which is subsequently described in more detail, the results would be more promising than those yielded by quinidine alone.

Auricular Fibrillation.—Until recently we knew of no remedies which would abolish auricular fibrillation; it is essentially a persistent condition. The treatment has been directed therefore mainly to control the rate of the ventricular contractions; such treatment still remains the most effective as a routine.

Digitalis Therapy.—Whenever the heart rate exceeds 100 per minute while the patient is at rest, digitalis or an allied drug may be given beneficially. It is to its effect on this form of cardiac disorder that digitalis owes its reputation, producing as it does a conspicuous slowing of the pulse rate. It slows the pulse rate in fibrillation as it does in flutter by the production or increase of heart-block, thereby impeding the passage of the rapid impulses from auricle to ventricle. An absolute control of rate is often established and the treatment consists first of all in maintaining the rate at or about normal. In this fashion the increased burden which the heart carries is reduced; with the reduction of rate, diastole is lengthened and the heart has more rest. It does not follow that a patient whose auricles are fibrillating should rest in bed; but it is advisable from many points of view that he should lie up while under the influence of digitalis, or at all events until the reaction of the heart to the drug is fully investigated. As a routine, the tincture is given to adults in doses of 15 to 20 minims (1 to 1.3 cc.) three times a day; if a reaction is not noticed within four or five days, the dosage may be increased and the remedy continued until symptoms, such as nausea, diarrhœa, headache, or pulse slowing, are observed. As a rule pulse slowing comes first; in other cases it comes simultaneously with other signs of intoxication; if the last have precedence and the ventricular rate remains high for several days, the oral administration of the drug should be discontinued. The dose is reduced as the heart rate falls, and often can be diminished to 5 or 7 minims (0.3-0.5 cc.) while the rate remains normal; not uncommonly, however, the rate begins to rise as the dose is reduced and a fixed dose of larger amount may then be required for long periods. In only a very few patients can the drug be withdrawn altogether without the original rapid rate returning. In general, adequate treatment demands heavy dosage initially, and subsequent, lighter dosage for long periods of time, it may be for the rest of the patient's life. The continuance or discontinuance of the drug is dictated almost entirely by the ventricular rate which prevails; enough digitalis must be given to bring the ventricular rate to normal; enough must be administered subsequently and daily to maintain this normal rate. Cumulative effects need not be feared so long as the ventricular rate is used to guide dosage and the rate is never allowed to fall excessively. In some few patients large doses alone will maintain a normal ventricular rate; these cases are less favorable. In a very few instances the heart rate fails to react; this is seen for the most part in senile patients and when the original rate is not very excessive. It is

unwise to maintain the rate at less than 60 for long; when there is profound slowing the condition may be precarious although the patient is in apparent convalescence. It is during periods of over-slowness and especially when, as a result of digitalis, the peculiar coupling of heart beats (Fig. 13) occurs, that unexpected death is encountered. In the presence of such a reaction strict precautions should be taken against sudden movement or emotional disturbance. It is best to maintain the patient upon pillows and to see that he is fed by hand during the whole of this period, and to employ the utmost care until the heart rate has risen again to normal. Excessive slowing and coupled action indicate overdosage; the condition is not seen if the dosage is properly regulated.

Fig. 28



Venous and radial curves in a case of fibrillation of the auricle, showing the curious coupling of the ventricular beats which occurs under the influence of large doses of digitalis. $\times \frac{1}{2}$. It should be noted that while the interval between large and small beats is always constant, the interval between small and large beats is very variable. This is a distinguishing feature in the particular type of coupling associated with fibrillation of the auricle. The venous curve shows the ventricular form of venous pulse.

In patients who are intolerant of digitalis, preparations of strophanthus or squill may be employed, each drug being pushed until a reaction is obtained, when the dose may be reduced. Intolerance to all these drugs is exceptional; in some patients digalen can be used hypodermically or strophanthin may be given intravenously. Strophanthin is also employed in cases of great urgency; the first injection of gr. $\frac{1}{250}$ in a 1 to 10,000 solution of saline is followed by a second and similar dose two hours later. As a rule the two injections suffice to reduce the rate in six or twelve hours, but a third injection of gr. $\frac{1}{250}$ or $\frac{1}{500}$ may be necessary.

Latterly, massive doses of tincture of digitalis have been advocated, a return to Withering's original plan of treating of dropsy. The idea is to bring the heart rapidly under the influence of the drug and the method is safe in the hands of those who thoroughly appreciate the nature of the disorder and have wide experience of its reaction to digitalis. The plan is to administer a single dose, approximately equivalent to 1 minim of the tincture to each pound of body weight. Thus 5ij are given to a patient who weighs 120 pounds. A reaction of the ventricular rate may be anticipated within twelve hours, and according to its degree the subsequent dosage is arranged. It is important in instituting therapy of this kind that a tincture should be used whose strength is known from *clinical* experience.

The continuous treatment in patients who are up and about is guided by the rate and the urgency of the symptoms. All hearts will not tolerate the same rate of beating; by a judicious employment of digitalis the rate may be maintained so that the burden which the heart carries is

not in excess of its capacity. Although patients with fibrillation often return to work, heavy work is not advisable. It should be moderated to meet the circumstances, and if any signs of returning failure appear, namely, increasing pulse rate, easy fatigue or breathlessness, further restrictions must be imposed. All female patients should be warned of the strain of pregnancy.

Quinidine Therapy.—While digitalis therapy still maintains its reputation as the safest and most reliable means of treating cases of auricular fibrillation in general, there is a small group of cases which may be treated in a different fashion. Quinidine is a drug having an extremely powerful action on the heart and, as has been shown, fibrillation may be abolished by its use, and the normal rhythm may be restored. But it is a drug which should not be administered lightly, owing to the frequency with which it produces undesirable effects. It is in fact still doubtful whether this form of treatment can be regarded as wholly justifiable; certainly it is not justifiable unless the cases are most carefully selected. The administration of the drug is definitely contraindicated in patients who give a history of hemoptysis or who show venous engorgement or much enlargement of the heart. Moreover the course of the treatment, when it is decided upon, should be followed, from hour to hour, by means of repeated electrocardiograms. Some patients will tolerate little quinidine, and develop symptoms of collapse or syncope on the usual doses. A preliminary testing dose of 2 gr. (0.13 gm.) should be administered to exclude such idiosyncrasy; if no unpleasant symptoms follow, a course consisting of 5 gr. (0.3 gm.) repeated three times daily, and twice at night may be tried, and the dose may subsequently be raised 50 per cent. throughout, if the desired effects are not seen and there are no toxic manifestations. In most patients such dosage lowers the auricular rate profoundly and raises the ventricular rate. When the auricular rate has fallen to 300 or 250 per minute an abrupt change often takes place, the heart resuming its normal rhythm. This reaction will be seen in about half the patients so treated. A strong criticism of the method is that the results are rarely permanent. Within a few months, fibrillation reappears in at least half the cases successfully treated originally. In only a few does the normal rhythm persist for twelve months or more. The adverse effects which may appear during the treatment are palpitation, headache, diarrhoea, giddiness and tinnitus; these, if not severe, will not prevent further treatment. A very high ventricular rate, or other adverse effects, such as a tendency to syncope, or urticaria will do so. If the normal rhythm is restored in patients who have clots lying attached to the auricular wall, these clots may be detached and give rise to embolism; it is for this reason that the drug should not be given to any patient who displays venous engorgement or much cardiac enlargement or gives a history of hemoptysis. Unquestionably the gain is great when the normal rhythm can be reestablished for long periods of time; but this happy event is seen in only a few patients. The continued use of quinidine in smaller doses, after the normal rhythm is established, does not seem materially to affect the after-history. Quinidine given in 2 gr. (0.13 gm.) doses has a limited value in warding off paroxysms of fibrillation.

Belladonna and similar drugs are contra-indicated in fibrillation; they raise the ventricular rate.

As in all cases of disordered heart action, attention should be given to general hygienic measures, and especially to the condition of the mouth and throat.

Slow Action of the Ventricle and Heart-block.—*Simple Bradycardia.*—Slow action of the whole heart requires no treatment, except in the cases in which the retardation produces anemia of the brain or threatens to do so. As a rule bradycardia (rate 50 to 60) is part and parcel of a general condition and the heart is reacting to extraneous influences; it is to the cause, whatever it may be, that treatment is applied in this circumstance. When the bradycardia is of high grade, or when the patient suffers from periodic *standstill* of vagal origin, and where no remediable mischief can be discovered along the course of one or other nerve, atropine or belladonna may be used; this treatment has met with success.

Heart-block.—The treatment of heart-block is regarded from the standpoint of the degree of the block and its duration. Where partial heart-block is of recent origin it is an index of active mischief; the subject of it should lie in bed and be searched thoroughly for the provocative cause. He should remain at rest until all signs of block have vanished or until it is known that the block has become permanent.

Partial heart-block when persistent calls for no immediate treatment; it is to be regarded as one sign of chronic myocardial disease, other signs of which are usually discovered. The patients who show it should be repeatedly examined. Signs of failure, if present, may suggest digitalis medication and the administration of this drug is not contra-indicated, even although it increases the degree of block.

The higher grades of heart-block are usually chronic and stationary and the habits of the patient are governed according to his general fitness or otherwise. Many patients of this class are up and are able to pursue some or all of their usual duties; but usually real bodily activity is impossible or inadvisable. A suspicion of an active or progressive lesion calls for rest and careful observation. Occurring in a syphilitic subject, thorough treatment with mercurials and iodides is indicated.

In those who suffer from convulsions, serious falls during the attacks should be guarded against; many of these patients have lost their lives by falling heavily. There are obvious occupations and sports which are positive dangers to all those who have attacks of unconsciousness. If the convulsions occur successively, it is well to confine the patient over the whole period of the disturbance and for some weeks afterward. Inquiry may reveal predisposing causes of the attacks and these may be remedied; among such causes gastro-intestinal disturbances are common. A few cases are on record in which atropine has seemed to check frequent seizures. But at the time of the convulsions, little can be done as a rule, beyond safeguarding the patient against injury. Drugs, such as strychnine, strophanthin, digitalin and amyl nitrite have been used in the hope of accelerating the ventricular rate; they seem to be without influence. Epinephrine injections have been used beneficially in a few cases.

Premature Contractions.—The presence of premature beats does not suggest a limitation of bodily exercise; it should not be allowed to interfere with the ordinary occupations of the patient. Restrictions are only necessary when associated symptoms or signs render them advisable. The patients may be reassured that such abnormalities are not serious, though the subjects of them may be reëxamined from time to time; reassurance often breeds the desired indifference. Sometimes the provocative cause, excessive smoking, flatulence, constipation, etc., may be identified and removed; but often the abnormality persists despite precautions and remedies. Quinidine is sometimes serviceable in ridding the pulse of this irregularity, when the latter is severe. No other drugs seem directly to influence the prevalence of premature beats except those which materially accelerate the heart, and these are undesirable. The symptoms, sometimes of a distressing kind, may be masked or abolished by bromides given in doses of gr. xv to xxx (1 to 2 gm.) or more a day. The ammonium salt is particularly valuable in tiding nervous patients over periods of exceptional disturbance.

Alternation of the Heart.—The presence of alternation, whatever its associations, is a sign of an overtaxed muscle. If the heart rate is normal or thereabout, the sign calls for drastic curtailment of work, and of all bodily or mental exertion. In sedentary people it is an indication that the hours of rest should be still further prolonged. It is one of the few signs of heart disease which forbids the administration of a general anesthetic, unless this is imperatively demanded to save life.

Unexpected and Sudden Death in Heart Disease.—When patients who are the subjects of heart disease die suddenly and unexpectedly, it has been our habit to search at the autopsy for evidences of clots, obstructing the pulmonary orifice, one or other auriculo-ventricular orifice, or a coronary artery; for we know that each of these accidents produces sudden and unexpected death. Yet at the majority of the postmortem examinations after the end has come abruptly, none of these lesions is discovered. It is in the highest degree probable that such patients succumb to a condition termed *fibrillation of the ventricles*. Fibrillation in the ventricles or *delirium cordis* is similar to the condition of fibrillation in the auricles; when it comes, coördinate systole in the ventricle is suspended and the muscle exhibits a continuous quivering and ineffectual movement. Its onset almost always spells death. Observation of ventricular fibrillation in the human subject is difficult for this reason. In animals under experimental conditions, it is of extremely common occurrence; the circulation is immediately brought to a standstill and the animal after a few gasping respirations and twitching movements of asphyxial origin remains permanently quiescent. The experiments of Levy have rendered it highly probably that unexpected death in chloroform anesthesia is of this kind. Fibrillation, be it understood, may appear in a perfectly healthy ventricle; but unhealthy heart muscle is especially prone to fibrillate, as we know from our experience of the auricle; and it is especially in cases of auricular fibrillation or in cases of paroxysmal tachycardia in which auricular fibrillation is also prone to develop, that sudden and unexpected death is often seen. It may occur in patients

who are under treatment with heavy doses of digitalis or an allied drug. At a stage when improvement is most apparent, when the ventricular action is slow, and when probably the coupled action (Fig. 13) which has been spoken of is present, the catastrophe occurs although convalescence was anticipated. A sudden movement or emotion may precipitate it, perhaps the patient rises in bed to fall immediately; a few gasping respirations, a little twitching of the limbs, rapidly developing cyanosis, and the pulseless patient is still. The postmortem fails to reveal the cause. This picture so closely resembles the outward signs in experiment, the circumstances in which the heart is placed are so suggestive, that it is difficult to remain unconvinced that fibrillation of the ventricles is responsible. Fibrillation of the ventricles is known to be the immediate cause of death when a coronary artery is ligatured; sudden death from embolism of a coronary artery in the human subject almost certainly comes in the same fashion.

Other possible causes of sudden death in heart cases have been mentioned already; vagal inhibition producing a permanent standstill has yet to be proved. The commonest cause of death from ventricular standstill is to be found in heart-block. Of the pathology of unexpected death in angina pectoris, we have little or no knowledge. Sudden death is not uncommon in those who exhibit alternation of the heart; in this condition, too, we do not know the manner in which the heart fails.

The following general treatises are mentioned for reference:

Wenckebach, *Arrhythmia of the Heart*, translated by Snowball, Edinburgh and London, 1904.

Mackenzie, *Diseases of the Heart*, London, 1920 (3d ed.).

Lewis, *Mechanism and Graphic Registration of the Heart Beat*, London, 1925 (3d ed.), *Clinical Disorders of the Heart Beat*, London, 1925 (6th ed.); *Clinical Electrocardiography*, London, 1924 (3d ed.).

CHAPTER XV

DISEASES OF THE MYOCARDIUM

By ROBERT H. BABCOCK, M.D., LL.D.

DISEASES RESULTING FROM DERANGEMENTS OF CARDIAC NUTRITION

BOTH the functional and structural integrity of the heart muscle is dependent upon a supply of healthy blood, any abnormality of which in either the constitution or amount must affect it more or less seriously. In simple anemia the heart may display weakness, dilatation, and increased frequency, whereas in pernicious anemia it may suffer degeneration. Again, abdominal derangements may be responsible for disturbed rhythm, while the toxins of acute specific fevers are capable of producing structural changes of a most disastrous kind. It is, however, the mechanical interference with its blood supply from coronary sclerosis which is the most surely injurious, and it is the myocardial disease of this origin that is most frequently encountered. Accordingly, whenever there is a structural defect with insufficiency of the myocardium, it is usually found to depend upon a disorder of cardiac nutrition.

Etiology—Acute Myocardial Degeneration.—*Acute Infections.*—For the most part it is the parenchymatous form of acute myocarditis which is seen as a result of acute infectious diseases. It is a manifestation of the action of toxins conveyed to the myocardium in the blood, and hence the likelihood of degeneration is proportionate to the intensity of the toxemia and not its continuance (Romberg). Of the infections likely to lead to myocardial degeneration the most prominent are *diphtheria*, *typhus*, and *typhoid fever*. The involvement may declare itself during the course of the fever, but in many instances it becomes apparent only after the subsidence of the primary disease.

Rheumatic fever, *scarlet fever*, *variola*, and *influenza* are also capable of producing this form of acute degeneration. In rheumatic fever, it is often the involvement of the myocardium rather than the endocarditis or pericarditis which renders the heart symptoms so serious. The injurious influence of *influenza* upon the heart muscle is a matter of every-day observation. Not only is the function of the organ disturbed in the course of the influenza, but signs of cardiac inadequacy may develop a considerable time after. The danger to life from such a degenerative process makes prolonged observation of the patient after convalescence from an attack of influenza highly important. *Gonorrhœa* is also to be enumerated among the specific infections which may occasionally be responsible for an acute myocarditis (Romberg).

Toxemia of Pregnancy.—Parenchymatous degeneration of the myocardium is a not infrequent postmortem finding in women who have

died during an attack of eclampsia. The lesion may vary from cloudy swelling to pronounced fatty degeneration. This condition of the heart muscle may be responsible for the symptoms of cardiac insufficiency observed in pregnant women suffering from toxemia, yet without convulsions. Bacon states that the symptoms of this form of myocarditis occur in about one per cent. of pregnant women.

Emboli.—Plugging of a coronary artery is a cause of acute degeneration and inflammation of the myocardium. If it is benign, the result is an area of acute necrosis, but if the emboli are of a septic nature, abscesses result. Such septic infarcts may occur in the heart walls as a result of suppurative processes in remote parts, but are most common with infective endocarditis.

Pyemia also predisposes to septic myocarditis, and hence it was that gladiators in the time of Galen were frequently found to have this form of acute myocarditis. Better surgical methods have rendered pyemia rare, and hence abscesses of the myocardium are infrequent unless in the course of puerperal infection or septic endocarditis.

Coronary Thrombosis.—A coronary artery may become gradually thrombosed, in which event the nutrition of the heart suffers with corresponding slowness, but when the blood supply to an area is suddenly shut off, degeneration follows rapidly, or, in other words, acute necrosis results.

Chronic Myocardial Degeneration.—1. *Intrinsic Causes.*—The conditions which predispose to slow damage of the heart muscle are many and varied. Some are clearly understood and plainly apparent, while others are indefinite and difficult of satisfactory explanation. In the former class are those factors which reside in the heart itself and hence may be called intrinsic. In the second, are most if not all of the conditions which, existing outside of the organ, may be called extrinsic and for the most part are really responsible for the intrinsic causes.

Coronary Sclerosis.—This is undoubtedly the one great intrinsic factor to which chronic changes of the myocardium are to be attributed. The sclerosis produces its effect on the heart muscle by its interference with the adequate supply of blood, not by the conveyance of toxins, although these may, in large part at least, be responsible for the sclerosis. The influence of coronary disease over the nutrition of the heart stands in direct relation to the degree of sclerosis and the rapidity of its development. Thus, if the lumen of the arteries be gradually narrowed, the result is the development of fibrosis or degeneration according to the degree of the coronary narrowing. If a thickened and narrowed branch suffers sudden thrombosis, the result is acute softening of the part supplied by that branch. Since a terminal twig possesses but a small calibre it may require comparatively slight thickening of its coats to induce thrombosis, and hence the frequency with which areas of necrosis are found in association with chronic changes in other parts.

Cases are now and then met with in which, despite pronounced changes in the coronaries, the integrity of the myocardium does not appear to have been seriously affected. In them either the arteries are still capable of conveying sufficient blood for the needs of the muscle, or the

vessels of Thebesius are able to carry enough blood into the myocardium to prevent disastrous loss of its nutrition.

In certain cases of the so-called senile heart, one is often astounded to find at autopsy such extensive and pronounced degeneration as to make him wonder how the organ performed its function without clinical signs of greater inadequacy than actually existed. The explanation can only be found in the failure of the degeneration to involve the conducting fibres, or in the absence of other intrinsic factors, which, if present, would surely have served to overpower the organ.

Valvular Lesions.—These bring about degenerative changes in the myocardium in the course of time. Their mode of action is probably manifold, but the main factors are perversions of cardiac metabolism and increased work. Disturbance of the heart's nutrition results from lack of sufficient blood on the one hand and defective removal of waste products on the other. Accordingly, all forms of valvular disease do not prove equally disastrous in their effects upon the heart walls. Aortic and mitral stenosis, especially the former, diminish the supply of blood sent into the coronaries because they lessen the amount discharged into the aorta; but in addition, mitral obstruction, through the stasis which it induces in the right heart, interferes with free flow from the coronary veins. Consequently it is in this form of valve disease that we meet with pronounced degree of *brown atrophy*.

Regurgitant lesions in the left side of the heart also occasion myocardial degeneration in a similar manner, but as they would not appear to interfere so seriously with cardiac nutrition, at least in their earlier stages, they seem to exert their effect largely through the increased strain on the heart walls. This is particularly true of aortic insufficiency.

The ventricle is called on for great increase of work, and at the same time demands increased nutriment both to maintain its nutrition *in statu quo* and to enable it to perform the extra work. If factors incident to its hypertrophy and dilatation prevent its receiving an adequate blood supply, then in time its fibres will undergo degeneration. But, however the degenerative changes in chronic valvular disease may be explained, they certainly are of great importance in bringing about the final break in compensation.

Heart Strain.—This may result from conditions incident to the manner of life and hence to be classed under the head of extrinsic causes, but the kind of strain here referred to is that due to conditions residing in the heart itself. Lesions of the valves tend to myocardial change because of the strain to which they subject the cardiac muscle, but there are other intrinsic causes independent of valvular disease. The healthy heart is capable of enduring an enormous amount of work without injury so long as its nutrition is maintained. But when in consequence of dilatation, however caused, the efficiency of the organ is reduced, degeneration is bound to ensue in time. Not only does the stretching of its walls augment its work by reason of the greater amount of residual blood left after each systole, but because of its enfeebled contractions a diminished supply of blood is sent into the aorta and coronaries. The nutrition of the myocardium suffers consequently and degenerative changes result even though

the coronary arteries be intact. It is probable that the hypertrophied heart secondary to prolonged high blood-pressure with or without seric is kidney changes can sustain the demands made upon it so long as its supply of blood meets its requirements, but when this becomes inadequate from any cause, then to heart strain is added degeneration, and myocardial incompetence soon declares itself. It is plain that heart strain as a factor in the production of chronic myocardial disease stands in close relation to and cannot be separated from nutritive disturbance and also various infective agencies.

2. *Extrinsic Causes*.—Some of these are manifestly extraneous while others are so intimately associated with the intrinsic factors as to make their separation difficult. These latter will be next considered.

Mode of Life.—This includes a great variety of influences of which some appear to involve heart strain, while others are harmful through toxic or nutritional effects. But under this head are embraced factors referable to business, social, dietetic, psychical, and other influences. In this class of cases, therefore, come instances of what Fraentzel termed Idiopathic Enlargement of the Heart. They are usually associated with hypertension in persons of both sexes who for years have led a strenuous life with insufficient recreation and exercise. Some are tireless men of affairs who lead too sedentary a life and perhaps whip up their flagging energies with stimulants and excessive protein diet. Others may be less strenuous but they are also too disinclined to physical exercise and habitually eat and drink more than they require. Accordingly they present instances of Fraentzel's *Luxus Consumption* which leads to abdominal corpulence, chronic nephritis, and abnormally high blood-pressure. Even when, as in some cases, blood-pressure is not excessive, it is probable that the intra-abdominal vessels, on which undue strain falls, have already begun to suffer sclerotic change.

In still other individuals obesity develops and eventually subjects the myocardium to degeneration from chronic overwork or fatty overgrowth. But in whatever manner the heart muscle is suffering, it is explicable by the mode of life rather than by any toxic or intrinsic factors. At all events we frequently see cases of myocardial incompetence in busy, strenuous men and women who give no history of any other etiological factors than their injudicious manner of overstoking and overdriving their bodily machinery.

Still another cause on which German writers, as Romberg, lay stress are neuroses, in particular neurasthenia and hysteria. The explanation is that owing to their extreme excitability and emotional instability they subject their cardiovascular system to sudden and violent strain, as in tachycardia from fear, anger, worry, etc. Such no doubt may be the explanation in some persons, but with some of these neuroses are factors such as chronic focal infections or previous acute illness.

Excessive Physical Toil and Hardships.—Considerable importance in the production of myocardial disease is attached to the severe physical exertion, together with the exposure and privations, experienced by soldiers, sailors, mountaineers, day laborers, coal miners, etc. Doubtless, the element of strain and malnutrition of the heart muscle comes into

play in such individuals, but one cannot ignore the influence of other factors, such as irregular habits and syphilis.

Alcohol.—This is a subject about which much conflict of views still exists. Experiments and pathological studies seem to prove that the direct injurious effect of alcohol is felt not by the cardiovascular system but by the stomach and liver. It is asserted that postmortem examination of drunkards fails to reveal sclerosis of the arteries and associated degeneration of the heart muscle. On the other hand, older writers point to degeneration of the myocardium found in inebriates. To the writer it would seem that if such changes are found in persons dead of chronic alcoholism they may be attributed not to the alcohol *per se* but to other factors intimately connected with the abuse of strong drink.

Immoderate beer drinking is held by German clinicians to produce disease of the heart muscle, not so much by reason of the alcohol as by the cardiovascular strain incident to the absorption and elimination of many liters daily. Rosenbach and Krehl attribute considerable etiological influence to the obesity which frequently results.

Syphilis.—Warthin has shown that the *Treponema pallidum* has a predilection for the tissues of the cardiovascular system. In both congenital and acquired syphilis areas of degeneration may be found in the myocardium, and syphilis may be the cause of this form of chronic myocardial degeneration far oftener than hitherto believed. It is well for the physician to sift to the bottom the possibility of syphilitic infection in all cases of cardiac inadequacy for which other obvious etiological factors are not evident.

Chronic Focal Infections.—Acute infections such as typhoid fever, influenza, and pneumonia may and often do set up changes in the blood-vessels and heart which in after years declare themselves as a slowly progressive degenerative process. So, also, a chronic infection like pulmonary tuberculosis can be responsible for coronary sclerosis and degeneration of the myocardium. It does not seem unreasonable to assume that chronic focal infections are capable of inducing degenerative changes in both bloodvessels and heart muscle. Cases have been reported of serious myocardial incompetence due apparently to no other cause than a chronic cholecystitis. In some of these instances the peripheral arteries were manifestly thickened and stiff and the heart gave evidence of being seriously degenerated. In some of these cases it may be that some infection many years earlier initiated the process, but in others it seems a fair assumption that the chronic gall-bladder infection led to the myocardial degeneration and dilatation, either through prolonged though slight cholemia or possibly by irritation of the splanchnic and consequent increase of blood-pressure. Disturbance of the sympathetic system may cause prolonged tachycardia and irregularity with resulting dilatation.

Chronic *appendicitis* as well as prolonged pelvic infection can disturb cardiac action seriously and in time bring about altered rhythm and dilatation, with interference with cardiac nutrition.

Hyperthyroidism may be appropriately mentioned in this connection since the cardiac disorder it induces is capable in time of causing dilatation and degeneration of a most serious nature. Chronic *tonsillar* infec-

tion may likewise be capable of leading to serious changes in the myocardium. We have slowly learned to recognize the disastrous effects that may follow prolonged focal infections, and their influence may be expended on the myocardium as well as on other structures.

Drugs.—It has long been recognized that fatty degeneration of the heart may result from phosphorus poisoning and the prolonged use of arsenic.

Exhausting Diseases.—Cancer, chronic dysentery, pernicious and even severe secondary anemia, and chronic suppurative diseases, lead to myocardial degeneration. In pernicious anemia the most extreme grade of fatty degeneration is often found, while in protracted suppuration this same form or amyloid change in the heart muscle may be found.

Morbid Anatomy.—Acute Changes in the Myocardium.—(a) *Acute Parenchymatous Degeneration.*—This condition is often spoken of as acute myocarditis, a term etymologically incorrect, since it implies an inflammatory and not a degenerative process. The condition results from the action of the toxins of acute infections. It is a diffuse process, characterized by cloudy swelling and granular degeneration of the muscle fibres. The myocardium looks pale and opaque, and is soft, flabby, and easily torn. Microscopically the fibres are swollen, their protoplasm more or less granular, and their striations indistinct.

(b) *Acute Interstitial Myocarditis.*—This occurs in two forms, purulent or simple, depending upon the cause. The former is the result of septic emboli, while the latter occurs in certain infectious diseases, *e. g.*, diphtheria, and typhoid fever, and in connection with acute pericarditis.

Purulent myocarditis is characterized by septic infarcts of variable number and extent. Occasionally these abscesses rupture into the endocardium or pericardium. These foci of suppuration are usually multiple and vary in size from a pin's head to a pea. They appear as whitish or grayish areas which on section are depressed below the plane of the cut. Fluid or semifluid pus may be found in the larger abscesses, while the smaller are seen microscopically to consist of masses of polymorphonuclear leukocytes surrounded by a zone of degenerating muscle fibres. Bacteria may often be demonstrated in these areas.

The simple form is very rare and is characterized by infiltration of the tissue with lymphoid and plasma cells. There is also considerable degeneration of the muscle fibres shown by swelling and destruction of their nuclei. Foci of such changes are more numerous in the wall of the left than of the right ventricle, and are generally situated close beneath the endocardium.

(c) *Acute Necrosis.*—This is a form of acute parenchymatous degeneration which results from sudden occlusion of a coronary artery by thrombosis or non-septic embolism. It is variously designated anemic necrosis, white infarct, acute softening, and myomalacia cordis. The degeneration is circumscribed and is most often found in that portion of the left ventricle and septum supplied by the anterior coronary artery.

The affected area has a yellowish-white or grayish-red color, is of an irregular wedge shape, and projects slightly above the surrounding level. The abrupt shutting off of the blood supply leads to coagulation

necrosis, which is soon followed by an inflammatory infiltration. Ultimately this necrotic patch becomes transformed into scar tissue.

Chronic Changes in the Myocardium.—(a) *Fibrosis, chronic interstitial myocarditis, fibroid degeneration*, are terms used to designate a condition in which the muscle fibres are replaced by fibrous tissue. The process may be diffuse, but is more often circumscribed. In the diffuse form there is a progressive atrophy of the muscle fibres with a corresponding increase of the interstitial connective tissue. When not very pronounced the condition is usually associated with a thickening or hypertrophy of the muscle wall. To the unaided eye the myocardium may, in the slighter degrees, look healthy, but when the fibrosis has led to thinning and dilatation, the heart is apt to have a paler appearance than normal and to cut with resistance.

In the circumscribed form there are smaller or larger areas of fibrosis, which in reality is a manifestation of Nature's attempt to conserve the myocardium against the injury wrought by some antecedent process. Thus it may be the final or reparative stage of an acute degenerative change, as anemic necrosis. The area becomes invaded by young connective-tissue elements which at length are converted into a firm fibroid cicatrix. The extent of such a focus is determined by that of the original lesion, but in most cases is not very great.

Areas of fibroid degeneration are most common in the wall of the left ventricle not far from its apex, in the upper two-thirds of its posterior portion in proximity to the auricles, in the papillary muscles of the left ventricle, and in the interventricular septum. When not very extensive or not disturbing cardiac rhythm they may not seriously interfere with the functional integrity of the heart, but in some instances they lead to localized dilatation.

(b) *Aneurism of the Heart.*—Under this term is designated, not that bulging of the semilunar valves sometimes seen as a result of endocarditis, but a circumscribed thinning and dilatation of the wall resulting from fibroid degeneration. The condition is usually single but may be multiple. The pouching occurs most often at or near the apex of the left ventricle, since here is the most frequent seat of fibrosis. The aneurism may be of such small size as scarcely to merit the term, or it may be so extensive as to constitute a sac of the size of the ventricle or of the heart itself. The pouch is very apt to be occupied by a thrombus, especially when it communicates with the cavity of the ventricle by a narrow opening. The formation of a coagulum within the sac is then conservative, as it tends to prevent rupture. In the majority the wall of the aneurism is unequal to the pressure of blood within it, and rupture takes place.

(c) *Fatty Degeneration.*—In this form of chronic myocarditis the heart muscle presents a generally pale appearance, with patches and streaks of yellowish-brown color, on which account it has been compared to a faded leaf or a tabby cat. The organ is much softer than normal, and can be easily penetrated by the finger. The areas of fatty degeneration are most common in the wall of the left ventricle near its apex, next in that of the right ventricle, in the interventricular septum, and in the wall of the right and left auricle in the order mentioned. The

muscle close beneath the endocardium is affected by this form of degeneration more than that underneath the pericardium, and the brownish or yellowish area may sometimes be plainly seen from within the heart cavities. Microscopically the protoplasm of the fibres is found replaced by fat-drops arranged in rows and situated at the junction of the transverse and longitudinal striations.

(d) *Rupture of the Heart*.—Fortunately this is rare, and yet it occurs with sufficient frequency to make an important cause of sudden death. The conditions predisposing to rupture are fatty degeneration and areas of acute necrosis, a focus of suppurative myocarditis, extreme fatty infiltration, and even a gumma of the myocardium. Fatal hemorrhage into the pericardium has followed rupture of a minute coronary aneurism. Rupture takes place most commonly on the wall of the left ventricle near the septum, but may be situated in any portion of the organ which has undergone serious degenerative change.

(e) *Fatty Heart*.—This term is used to designate fatty degeneration or an excess of adipose tissue. In well-marked cases of the latter kind there is an overgrowth of subepicardial fat which may cover the heart like a blanket and conceal the muscle beneath, the *cor adiposum* of old writers. There is also an infiltration of fat between the muscle fibres which in places have become atrophied or may be the seat of fatty degeneration. In extreme instances the heart is relaxed and its cavities are dilated. Fatty infiltration is often combined with general obesity.

When the myocardium presents chronic degeneration, it may present a picture made up of these varying conditions—fibrosis, fatty degeneration and fatty overgrowth. As these changes depend upon disturbances in the nutrition of the myocardium, more or less evidence of coronary sclerosis is generally found. If there are associated changes in the kidneys and arteries, the heart is likely to be hypertrophied and dilated. When the sclerosis is most marked in or limited to the coronary arteries, the organ may be markedly atrophied and the myocardium furnish a good picture of brown atrophy. This is seen especially in the so-called senile heart.

(f) *Fragmentation and Segmentation of the Myocardium*.—This condition, first described by French writers, has received much study by pathologists. Fragmentation is so called because the fibres are found fractured, the cells being broken at the level of the nuclei. In segmentation there is a separation of the fibers in their cement substance. The two conditions may be combined in the same specimen. This change in the myocardium may occur in the death agony or before dissolution, and prove a clinical and pathological entity of importance, although very difficult, if not impossible, of recognition during life.

Other Rare Forms of Degeneration.—(a) *Amyloid Degeneration*.—This is sometimes met with in the same class of cases as is this change in other organs. It occurs in the interstitial connective tissue and in the coats of the bloodvessels, but not in the muscle fibres.

(b) *Hyaline Transformation*.—This may occasionally be seen after protracted fevers. The fibres are swollen, homogeneous, translucent, and have nearly or quite lost their striations.

(c) Lastly, the muscle fibres may become infiltrated with lime salts and be the seat of *calcareous degeneration*, which is very uncommon.

Symptoms. — **Acute Parenchymatous Myocarditis.**—These depend on the nature and extent of the myocardial change. It may not declare itself by clinical signs and may only be recognized postmortem, or the disease is not suspected until the sudden death of the individual. In other cases there are symptoms sufficiently pronounced to permit of their correct interpretation, while in still another group the symptoms due to the myocarditis are obscured by and very likely referred to some associated and easily recognized affection, as endocarditis or pericarditis.

Acute myocarditis seems to be especially dreaded in *diphtheria*, but according to Romberg and Schinaltz its symptoms occur in only from 10 to 20 per cent. of cases. When, however, symptoms so arise they are likely to be serious. They may appear at any time from the close of the first to that of the fifth or sixth week, though most often in the second or third after the onset of the illness.

Examination of the heart at this time is likely to disclose feebleness or even absence of cardiac impulse, increase of relative dulness transversely, and marked weakness of the tones. The first sound at the apex may be muffled and toneless, or it may be audible as a short tone which is accompanied by a more or less faint, blowing, systolic murmur. This murmur is generally restricted to the mitral area and denotes not an associated endocarditis necessarily, but muscular mitral insufficiency. In reality it is a dilatation murmur which is heard, and hence it may wholly disappear after the cardiac asthenia has been recovered from and the left ventricle has returned to its normal size.

Signs of stasis are not so pronounced in the liver and other viscera as to attract special notice, and save for pallor or cyanosis the patient may not, to the inexperienced observer, betray by his appearance the serious state of his circulatory apparatus. On this account cases with serious damage are occasionally overlooked, and children convalescing from *diphtheria* are permitted to play about before the heart is equal to the exertion. It is probable that if the heart had been critically examined in the unexpectedly fatal cases it would have displayed some features indicative of left ventricle weakness and dilatation.

In *typhoid fever* acute parenchymatous myocarditis may be shown by emptiness and compressibility of the pulse (low systolic blood-pressure) rather than by marked frequency. In those cases in which myocarditis seemed to the writer to exist, greater rapidity of the heart's action was noted than is usual in typhoid fever, yet not so great as might have been expected in grave cardiac asthenia. The first sound at the apex is likely to be strikingly wanting in clearness and strength, although an actual murmur may not be detected. Careful percussion may determine an increase in the area of dulness out of proportion to the clinical evidence of myocardial inadequacy. The objective manifestations of the myocarditis are to be sought, therefore, in the characters of the pulse and in the auscultatory findings rather than in venous stasis.

Influenza often causes signs of myocardial weakness from acute parenchymatous degeneration. The pulse is accelerated and feeble, while the

heart tones are correspondingly deficient in strength. These signs may appear during the primary affection or be first noticed after the individual has resumed his activities. During the acme of the illness the weakness and rapidity of the pulse are apt to be attributed to the fever and prostration. But upon the patient returning to work he is found to be a little short of breath and easily fatigued. There may be a slight or vague sense of discomfort in the precordium rather than of positive pain, and now and then there may be palpitation or vertigo. The color of the face is pale or faintly cyanotic and the heart is found rapid, perhaps irregular and intermittent. The pulse is of low tension and the apex beat is indistinct or displaced to the left. The tones are weak, especially the mitral first sound, which may be accompanied though not obscured by a soft murmur. Comparison of the pulse-rate and systolic blood-pressure before and after exercise generally discloses more or less pronounced evidence of defective myocardial response.

With rest in bed and appropriate treatment some of these patients recover and the heart no longer exhibits signs of inadequacy. In other cases the acute seems to pass into a chronic myocarditis, and the pulse never regains its former regularity and strength. The heart is permanently damaged and there may be a persistent apex murmur.

In *rheumatic fever* the degeneration of the cardiac muscle is very apt to be masked by the signs and symptoms of an associated endocarditis. When an acute endocarditis appears in children there is generally pronounced dilatation of the chambers most nearly concerned. We are wont to refer such enlargement to mechanical causes, but it is probable that pronounced dilatation does not occur unless acute myocarditis also exists. If the heart muscle is not seriously affected in its nutrition, a valvulitis is speedily compensated for by the development of hypertrophy in the chamber which has to bear the brunt of the strain. Therefore, when in rheumatic fever a degree of dilatation develops which is disproportionate to the apparent endocardial mischief, acute parenchymatous myocarditis may be assumed.

If the heart walls are extensively damaged the rhythm of the contractions is likely to be disturbed. The pulse is apt to be accelerated and to display more or less irregularity in time, force, and volume. Greater disturbance of the heart's action results from comparatively trivial exertion or mental excitation than should be the case. The patient becomes noticeably pale and may have an anxious look, yet he denies the presence of pain or speaks of a dull, oppressive feeling at the heart rather than acute distress.

If such patients recover at all, it is only after weary months of scarcely appreciable improvement. Not only has the nutrition of the myocardium been affected, but that of the organism in general has been seriously compromised. In particular it is the kidneys which in these acute infections are likely to share in the inflammatory process. This nephritis disappears long before the myocardium acquires sufficient hypertrophy to denote a compensatory reestablishment of its power. Even then, after the individual has returned to his previous manner of life, more or less arrhythmia or tachycardia is likely to persist.

Acute Interstitial Myocarditis.—Cardiac symptoms are very likely to be masked by those of the underlying condition. When, however, the myocardial inflammation dominates the scene, the clinical picture is very likely that of malignant endocarditis. There may be slight rigors, an intermittent pyrexia, and enlargement of the spleen. The heart's action is rapid and feeble and the area of cardiac dulness may be increased. The sounds are apt to be clear but weak, and murmurs are wanting. In some cases there may be nothing to indicate the critical state of the myocardium and the condition is recognized only at autopsy. In some of these cases the existence of the suppurative myocarditis is first revealed by the symptoms of collapse, the heart wall having ruptured into the pericardium. If an abscess has discharged its contents into the blood stream, there are the phenomena of septic infarcts in distant parts, skin, kidney, spleen, liver or brain.

From the standpoint of symptomatology, acute myocarditis of either form may be divided into two classes: (1) Cases in which symptoms pertaining directly to the heart are absent or so obscure as to be overlooked; (2) cases in which evidence of cardiac incompetence is too conspicuous to be overlooked or may be discovered if sought for. For the most part it is the first class of cases which are especially dangerous and for the discovery of which the physician should be always on the lookout when treating any case of acute infection. He must not be deceived by the want of obvious signs of venous stasis, for these are more apt to be absent than present. The reason for this is conjectural. It may be due to toxic paresis of the vasomotor centres as suggested by Romberg, or under the influence of a splanchnic neuritis (Veronese) there may be stasis within the great veins of the abdomen with corresponding emptiness of the superficial veins. The physician should also be on the watch for slight yet significant signs of myocardial weakness, such as low blood-pressure with feebleness and emptiness of the pulse rather than marked frequency; perturbations of rate and rhythm out of proportion to the degree of effort that evoked them; sudden and alarming periods of weakness when the pulse grows rapid and almost imperceptible; listlessness and weakness on the part of the patient and apathy or marked restlessness. Striking pallor of the countenance, vomiting and precordial pain are symptoms which, if not always present, are yet very significant and should excite apprehension. If combined with some of the evidences of myocardial incompetence, they render the existence of acute myocarditis highly probable.

The *course* may be quite diverse both as regards onset and duration. It may set in suddenly and under symptoms of ever-increasing severity lead to death in a few days or weeks. On the other hand, the myocarditis may develop insidiously and remain latent up to the moment of unexpected death; or there may be periods of entire absence of symptoms which alternate with times of alarming symptoms and all the appearances of impending death. Lastly, the affection may first declare itself by signs of cardiac inadequacy of greater or less severity, several weeks after all thought of danger has passed.

Chronic Myocarditis.—There is much diversity in detail presented by the clinical picture of *chronic myocardial degeneration*, yet different

as these points may be, the background remains ever the same, namely, cardiac incompetence. The differences are determined by the seat and extent of the morbid anatomical changes as well as by their exact character and their association with degenerative changes in other organs. Cases falling under this head may be variously classified according to their pathogenesis, their pathological peculiarities, or their clinical manifestations. An etiological grouping would be very desirable, but seems impracticable with our present knowledge, since we are not able to decide which of several factors may be the essential one. A classification based upon the precise nature of the myocardial change is likewise not feasible since various changes generally exist in each case. We are confined, therefore, to a division based on clinical manifestations.

Two main groups may be distinguished: (1) Those in which symptoms referable to the heart are latent or so disguised as to escape recognition, and the existence of heart disease is first declared by sudden death; (2) those in which symptoms of cardiac inadequacy are more or less conspicuous. The cases in this second group may be subdivided according as symptoms are distinctly cardiac or are blended with others attributable to disease of other structures. In reality it is the union of several such interdependent conditions which accounts for the diversity in the details of the clinical picture. Accordingly, this arrangement of cases will be maintained so far as is compatible with clearness and accuracy.

Latent Cases.—In this group belong the occasional instances of sudden and unexpected death among middle-aged or elderly and apparently robust men. They are often reported as cases of apoplexy, but are in reality instances of cardiac paralysis or sudden heart failure. The Germans call it “*herzschlag*” (heart stroke), and appear to recognize its exact nature more often than is done in this country. In instances of this kind it may be that a man engaged in conversation or perhaps at the end of a meal, in whom nothing abnormal has been noted, falls over dead. In the press reports of these cases it is generally said that the deceased was in excellent health and had experienced no symptoms that indicated the existence of heart disease. Such is doubtless true in many instances. In others there have been symptoms which were attributed to indigestion, nothing more. It is quite likely, nevertheless, that if these victims had been critically examined they would have exhibited some of the signs which point to the probability of chronic myocarditis.

The reasons for the latency of these cases are to be found in the insidiousness of the changes going on in the heart muscle and in the location of these changes. Their seat may be such as to cause a perpetually irregular pulse or to interfere with the conducting fibres and lead to heart-block. Even though this latter may not occur, perpetual arrhythmia may mean dangerous heart weakness.

On the other hand, there may be a condition of hypertrophy with dilatation of the left ventricle, the former condition having predominated for years and thus precluded subjective symptoms. The degenerative process slowly and insidiously saps the strength of this hypertrophied wall, and at length it becomes incapable of withstanding high intraventricular blood-pressure. So at length comes a moment when under

the inhibitory stimulus of some strong emotion, an unwonted or hasty physical effort, a hearty meal, etc., blood-pressure within the degenerated ventricle is raised to an unsupportable degree and the heart stops in diastole. Such a time of danger may arise in the life of any person whose myocardium has become degenerated.

Examination of the heart in these latent cases would probably reveal signs of general cardiac hypertrophy. Although by reason of the capaciousness of the chest the area of heart dulness may appear natural, still the increase of blood-pressure and thickening of the arterial coats evince the strain on the heart, while the intensity and ringing quality of the aortic second tone bear confirmatory testimony.

In these cases there is more or less acceleration of the pulse, or a slight amount of breathlessness on exertion to which the individual pays no heed, having attributed it to his increasing weight or age and, therefore, supposed it quite natural. On brisk exercise also systolic blood-pressure does not rise and remain up as it should after the pulse has fallen to its former rate. Such, at all events, are the evidences of incipient, cardiac incompetence which may be detected in men who consider themselves in perfect health.

Cases with High Blood-pressure and General Cardiac Hypertrophy.—It must not be supposed that the cases grouped under this head monopolize these features of the pulse and heart. They only constitute the findings which stand forth most conspicuously. Fraentzel designated them idiopathic enlargement of the heart to distinguish them from instances of hypertrophy secondary to chronic valvular disease. In the writer's experience they are most common among the large-framed, energetic men who are engaged in office work and, under the influence of good living, early develop a degree of obesity which puts an injurious burden upon their circulatory apparatus.

Slowly and insidiously the myocardium has been answering to the heavy demands made upon it by ever-increasing thickness of its walls, not a true hypertrophy of its muscular elements, but a false hypertrophy in consequence of the growth of connective tissue. To whatever special factors the augmentation of blood-pressure is to be ascribed, the fact remains that for an indefinite time it has been high. There may or may not be demonstrable thickening of the arteries, and some degree of renal change may be shown by urine containing a few granular and hyaline casts. Now and then a trace of albumin may be detected, but on the whole the renal elimination is satisfactory.

Year by year the elevation of blood-pressure becomes more pronounced, and little by little the development of fibrous tissue undermines the power of the myocardium. At length symptoms begin to declare the strain to which the heart is slowly yielding. In some cases it is *dizziness* which first attracts attention. The sensation is slight and transient, perchance, but it occasions uneasiness. A physician being consulted, the state of the heart and vascular system is recognized. Measures are prescribed for reduction of blood-pressure and the patient is relieved of his annoying vertigo. In some instances the excessive blood-pressure leads to a severe and almost uncontrollable attack of epistaxis, and the symptoms are relieved for a time.

In other cases it is *breathlessness on exertion* which is first noticed. This, too, may be lessened or removed for a time, but, as a rule, it does not vanish altogether. Associated with the shortness of breath may be a sensation of weight or *fulness in the precordium*, or there may be a dull ache or pain in the upper sternal region whenever the man walks at more than a very moderate pace.

In still other cases the initial symptom is *palpitation*. It is often described as a thumping or pounding of the heart which attracts notice during exertion or at night. In some instances the individual is unable to lie on his left side because of this sensation. Not infrequently breathlessness is experienced as well as palpitation or vertigo. In other cases the patient complains of unwonted weakness or of *epigastric fulness* or pain which he attributes to indigestion. His conviction of its being only a digestive disorder is increased by eructations or by aggravation of his sensations after meals. If he is a little short of breath, especially after eating, he regards it as due to bloating with wind.

In some one of these various ways this type of myocardial incompetence first makes its advent known. As time goes on the cardiac inadequacy increases and the individual attends to his ordinary duties with ever-growing difficulty. Usually at this time it is the shortness of breath which incapacitates him. He is aware of decreasing strength and endurance, but it is the dyspnoea which really torments him. He is noticeably short of breath even when at rest, but it is when he walks about or goes to bed at night that he suffers the most. Things go on from bad to worse and at last he gives up and stays at home.

Examination of the heart now discloses plain signs of myocardial incompetence. The pulse is more or less accelerated, usually regular, and of high tension. It is difficult to compress the artery and high systolic and diastolic blood-pressures are found. The radial arteries roll under the finger but are not always markedly sclerotic. There may not be pitting, or even puffiness, of the ankles.

The apex beat if perceptible is found in the fifth or sixth intercostal space, outside the nipple line, and 5 or more inches to the left of the median line. There may be epigastric pulsation of variable strength according to circumstances. Deep-seated and superficial dulness is increased in all directions but chiefly to the left, and the outline is quadrangular, indicating general enlargement. The heart sounds are somewhat enfeebled, especially the mitral first, which is often accompanied by a blowing murmur. The pulmonic second tone is likely to be accentuated and the aortic second sound is ringing.

The lungs are resonant, but at the posterior bases rales of chronic bronchitis or hypostatic congestion are heard. Now and then there may be a slight amount of fluid in the right pleural cavity. The liver is enlarged. The urine is diminished in amount, of increased specific gravity, and may contain a variable percentage of albumin. If casts are present they are granular, or both granular and hyaline.

The *course* is henceforth either steadily from bad to worse, or, under treatment, tends for a time to improvement. In the former event, œdema increases until general dropsy supervenes; the dyspnoea becomes

orthopnoea, with possible paroxysms of veritable air hunger. The heart grows more and more incompetent, with possible irregularities in force and rhythm. Hepatic stasis augments to the point of epigastric pain and tenderness. The lungs grow distinctly œdematous, and the urine is scanty and highly albuminous. The picture has now become that of extreme myocardial insufficiency. The end comes slowly and gradually, or, after weary months, the worn-out heart stops suddenly.

Should treatment improve the condition, the reinstatement of heart power is but partial and often transitory. In the case of a rich man, a journey to Bad-Nauheim may be succeeded by such improvement that he is able to return to his office. The less fortunate workingman finds so much relief from rest in bed in a hospital ward, that when discharged he flatters himself he can resume hard work. In either case the man sooner or later again grows conscious of the approach of his old enemy. This time the symptoms, if they yield at all, do so with greater reluctance than before. Thus, with discouraging repetitions, the patient drags on until death terminates the unequal fight, either abruptly and unexpectedly, or in the midst of all the phenomena of extreme myocardial inadequacy. In not a few instances it is apoplexy, pulmonary œdema or secondary pneumonia which closes the scene.

Cases Associated with Chronic Nephritis.—In the class of cases just depicted the urine is not normal, but if the kidneys are diseased their condition is subordinate to that of the heart. In others, the primary disorder is a chronic nephritis, commonly of the interstitial variety, but many times of a mixed kind. There has been abnormally high tension for years, which, directly prior to the breakdown, may reach figures of 225 or even 260 mm. It is this excessive peripheral resistance which is responsible for the myocardial inadequacy, and when at last serious symptoms set in they may be in reality those of cardiac rather than renal incompetence, although the latter supervenes in time.

Usually the first symptom is shortness of breath on exertion. In some cases it is vertigo which appears especially while walking. As time goes on this breathlessness grows into outspoken dyspnoea. It is apt to be associated with unwonted nervousness and more or less decrease in strength. Some patients suffer to a great degree from dyspnoea, nervousness, and insomnia. In search for relief they tramp and work until exhausted, and then go to bed in hope of repose.

If the heart is examined at this time, it is found hypertrophied and beating with increased frequency in the attempt to overcome the resistance offered by the abnormal pressure. The sounds may be clear but the first at the apex is short and valvular and the second sound doubled so as to produce a gallop rhythm. The aortic second sound is loud and ringing, and in some cases this is the most marked feature. Accentuation of the pulmonic second tone indicates the heightened blood-pressure in the pulmonary vessels, but other signs of congestion within the lungs are not very manifest. The excessive resistance in the aortic system is overpowering the myocardium.

Appropriate treatment ameliorates the condition for a longer or shorter period. Yet the pulse is found habitually tense and too rapid. Hyper-

trophy still predominates, but is slowly yielding to dilatation. There may be no pronounced cardiac symptoms, and yet he is aware, every now and then, of breathlessness or palpitation and of a want of his old-time vigor and endurance. At length, either in consequence of injudicious physical effort or because the degenerated myocardium has yielded to the dilating force of the persistently high blood-pressure, the patient's dyspnœa reasserts itself. From this point forward the symptoms are those of increasing myocardial incompetence.

Examination of the heart now shows a combination of hypertrophy with dilatation which involves chiefly the left ventricle. The area of deep-seated dullness is not quadrangular, as in the preceding group of cases, but extends to the left to a variable distance outside the nipple line. The apex beat is diffused and uncertain, and the palpating hand appreciates an indistinct doubling of the impulse. Upon auscultation, this diastolic tap is found to correspond to a reduplication of the second sound, giving a more or less characteristic gallop rhythm. There may or may not be a systolic apex murmur depending upon the degree of dilatation.

The pulmonic second sound is intensified and the aortic second may be diminished, but more sharp and metallic than normal. The pulse is of increased frequency, 110 to 125, and regular or now and then intermittent. The radial artery is hard to compress. The sphygmomanometer records hypertension with more or less distinct alternation. The liver is apt to be palpable and may be tender. In many cases it is firmer and thinner than in pure congestion of the organ being more or less cirrhotic. The urine is less abundant and usually contains albumin and casts. The ankles may pit slightly, but in the beginning of this final struggle are not markedly œdematous. In some instances dropsy is wanting.

The course is now very like that in any other case of cardiac inadequacy, but the patient's dyspnœa, restlessness, nervousness, and increasing weakness are apt to be more pronounced than in the incompetence of valvular disease. Later developments are a general dropsy and, finally, ascites.

Not infrequently this state of malnutrition brings on acetonemia or a form of toxemia which is an *inanition toxemia*. The patient is not actually delirious but is drowsy and not clear in his mind, while at night he may show mental rambling and sometimes excitement. In some cases the toxemia is of *hepatic* origin and closely simulates uremia. The breath is heavy and foul, and the sensorium is decidedly obscured. The breathing may assume a Cheyne-Stokes type.

The heart is now still more dilated; a tricuspid, regurgitant murmur is added; the external jugulars pulsate visibly; the liver is still more engorged; the pulse is irregular, intermittent, or too arrhythmic to be accurately counted. It is feeble and the sphygmomanometer may show an abnormally low systolic pressure over an abnormally high diastolic pressure, giving a diminished pulse-pressure. The condition is pitiable and the fatal termination is only a question of time. Death may come suddenly when the condition seems unchanged, certainly a very merciful ending, or the feeble spark of life may simply flicker out; or uremic coma

may terminate the struggle; or the exitus may take place in consequence of pulmonary œdema.

Some of these nephritic cases show wonderful tenacity of life so far as the heart is concerned. According to the writer's experience they are those which display predominating dilatation of the right heart. The left ventricle is also dilated and the mitral valve leaks, but the behavior of the organ as a whole points to degeneration and dilatation of the auricles and right ventricle as the leading feature. The action of the heart is so irregular that one can aptly term it *delirium cordis*.

The excretory ability of the kidneys is greater than might be supposed from the degree of albuminuria, and, unless too greatly damaged, these organs may respond well to such a remedy as diuretin. Nevertheless, it is the myocarditis even more than the nephritis that is surely dragging the patient to his grave. Part of the clinical picture is owing to the albuminuria, it is true, but it is the incompetence of the heart muscle which is mainly responsible for the symptoms. That it is not stasis, solely, which causes the dropsy in all cases, is proved by its diminution or disappearance after chloride of sodium has been withdrawn from the dietary.

In other instances the œdema is so slightly influenced by a non-chloride diet that venous stasis must be regarded as a principal factor in its production. It is these cases that are so intractable to treatment, and pursuing a steadily downward course terminate after months at the outside. There is a vicious circle of conditions which precludes all hope of recovery, but the fact that other than palliative measures are without avail from the moment the abnormally high gives way to low blood-pressure, proves that the chronic myocarditis is the reason for our defeat, if, indeed, it were not so from the outset.

Cases with Angina Pectoris.—These occur chiefly in elderly men although not limited to the male sex. This complaint receives consideration elsewhere in this work and here is discussed briefly. Worthy of special comment is the fact that when a physician is consulted for this complaint by an individual in the late fifties or early sixties he is apt to be struck by the paucity of clinical findings indicative of definite myocardial pathology. The pulse is commonly somewhat accelerated but regular and the accessible arteries may show only slight changes. The radials and carotids feel stiffer than they should normally and the writer has noted in some cases that the subclavian arteries stand out more noticeably above the clavicles than is usual in younger persons. The blood-pressure, particularly the diastolic, may be found distinctly raised, as for instance 180 mm. over 110 or even 120. More or less hypertrophy of the left ventricle may be detected, while an electrocardiogram records distinct left ventricle preponderance. Auscultation may or may not discover a systolic bruit in the aortic area, rarely at the apex, but often the heart tones show only some alteration in intensity, as a ringing aortic second or diminution of the mitral first sound. Urinary changes may or may not exist, but if the blood-pressure is strikingly high, 200 or more over 120 or 130, albumin and casts are likely to be found.

Whenever there is pronounced substernal pain with oppression, induced by walking, excitement, worry, etc., most clinicians attribute

it to coronary sclerosis with consequent changes in the heart muscle. That such pathological alteration is present is probably true in all cases, but the writer desires to voice his adherence to the view of Sir Clifford Allbutt; namely, that the predominant etiology, barring cases of coronary thrombosis, is sclerosis of the ascending limb of the aorta. According to Allbutt the suprasigmoid portion of the aortic arch is richly supplied with sensory nerves which, when the coats of the vessel are stretched from increased internal pressure, give rise to the symptoms. In such cases the writer has generally been able to discover more or less marked indication of widening of the aortic arch, such as dulness over the manubrium with thickening of the coats of the cervical arteries, a ringing aortic second tone and a systolic murmur. The fluoroscope has almost invariably corroborated these findings.

That increased intra-aortic pressure and atheroma of the vessel explain the causation of the angina in such cases seems to the writer proved by the gratifying results of treatment in a number of instances. Whatever be the precise etiology this symptom is most serious since it carries with it the possibility or likelihood of sudden death. Not many months ago a man displaying this distressing malady with the above findings was seized with an unusually severe attack in a hotel, and died only a few hours after having been warned of the possibility of just such an occurrence.

Patients presenting typical signs of cardiovascular change and the characteristic picture described by Heberden are not difficult of recognition, but when the location of the pain is precordial rather than substernal, and when associated with areas of intercostal tenderness, the precise nature of the symptom may be difficult of determination. Nevertheless, when there are findings suggestive of or warranting the diagnosis of chronic myocarditis the symptoms may generally be regarded as angina pectoris.

Senile Heart.—One not infrequently encounters old people of both sexes whose hearts, if examined by the pathologist, would display the changes of myocardial degeneration, yet who enjoy a surprising state of health. The pulse may be more or less irregular and sometimes very arrhythmic. The blood-pressure may be increased to 165 mm. Hg. or higher, and the arterial coats feel stiff or even beady. The apex beat is displaced outward and downward in consequence of combined hypertrophy and dilatation. The sounds are accompanied by systolic murmurs both at the apex and in the aortic area, while the second tone is ringing and possibly impure. The urine shows changes that go with this cardiovascular degeneration, namely, nocturnal increase, low specific gravity, a trace of albumin at times, and granular and hyaline casts. Stasis in the portal vessels is not marked, but digestive disorder shows itself by flatulent distention of the bowels and eructations.

The majority of such old persons keep tolerably well so long as they follow the even tenor of their way or are kept on appropriate doses of digitalis. So soon, however, as they overdo in some manner, and, particularly if they contract bronchitis or some other ailment, they show at once how little resisting power they possess. The heart at once evinces

its intrinsic feebleness, which it is important to recognize early and endeavor to arrest before it grows more serious. These patients are very likely to succumb to pneumonia or die suddenly. In many of the cases the chronic myocarditis is but an incident in old age, and, so long as the heart is potentially equal to its ordinary work, it requires nothing more than protection against additional demands. In other cases cardiac symptoms may make their appearance and pursue the usual downward course. In not a few instances these old hearts rally in a wonderful manner, under skilful management, and then may be bolstered along for months and even several years.

Cheyne-Stokes respiration may appear and persist in a more or less typical form. In other instances it may disappear after a time or show itself only when the patient is asleep. It does not depend upon the state of the myocardium so much as upon the condition of the vessels in the medulla, and hence the blood supply to the respiratory centre.

Precordial pain may or may not be experienced, but in the cases considered typical illustrations of the senile heart it is the exception. In a few instances angina pectoris has been a leading feature and in others there has been a dull pain in the cardiac region, which, however, was subordinate to other symptoms.

The *pulse* presents all possible variations in rate and rhythm. It is more apt to be too frequent than too slow, and there may be paroxysms of tachycardia of uncertain duration. When these subside they leave the patient much exhausted. They may be an expression of cardiac asthenia and after several months of treatment the pulse, previously very weak and arrhythmic, may become regular and fairly strong. As already stated irregularity of the heart's action is a marked feature of many cases. In other cases irregularity shows itself only during some physical effort and then evinces the potential feebleness of the myocardium.

Stokes-Adams Syndrome.—Abnormal slowness of the pulse, to which earlier writers attached so much importance in the diagnosis of fatty degeneration of the heart, is far less common in chronic myocarditis than is increased frequency. The cases in which the writer has observed habitual bradycardia were generally in middle-aged men with enlargement of the heart. Now and then a case is encountered in which the myocardial incompetence is attended with bradycardia of such striking character as to merit a separate clinical grouping.

These cases are marked by findings, which, originally described by Stokes and Adams, have been named after these eminent Irish observers. These cases are characterized by such extreme slowness of the heart's action that the brain is inadequately supplied with blood, and hence the individuals suffer also from vertigo or even syncope. In some instances the seizures so closely simulate an epileptic fit, that they have been mistaken for convulsions of this nature or thought uremic. Although not confined to persons of middle or advanced age, still these attacks of bradycardia are most often seen in individuals whose various organic lesions, if not their actual age, place them in the category of senility. These patients usually, but not always, die suddenly, probably from

heart-block during one of their attacks. Now and then this bradycardia is heart-block of vagal origin, in which event atropine restores the heart-rate, for a time at least, to normal.

Rupture of the Heart.—Chronic myocarditis occasionally terminates abruptly through rupture. The mishap is announced by symptoms denoting grave cardiac failure: precordial pain or oppression, rapid, feeble pulse, cold extremities, and pale, anxious countenance; in short, the symptoms of collapse. The area of heart dullness is increased, and the tones are distant and weak. Death supervenes after a shorter or longer period, from a few minutes to many hours, and a correct diagnosis is usually made only at autopsy.

Aneurism of the Heart.—Symptoms by which this condition may be recognized are seldom occasioned. Such as exist are attributable to myocardial inadequacy. If the aneurism be very large it is recognizable by the fluoroscope or may so modify the outline of cardiac dullness as to lead to a correct diagnosis. In very exceptional cases there may be bulging of the chest wall in the vicinity of the apex, and this tumor may pulsate so as to simulate a double apex beat. The symptoms are in effect those of cardiac dilatation. Such cases generally terminate in rupture without being recognized clinically.

Cases Simulating Valvular Disease.—It is not very uncommon to encounter individuals of forty or over who manifest symptoms of cardiac insufficiency, and who, on examination, are found to have signs of mitral or aortic valve disease. Sometimes it is a mitral systolic murmur, sometimes an aortic diastolic murmur. Occasionally there is evidence of slight stenosis associated with the incompetence of the mitral valve. There is no clear history of rheumatism, but there is often high blood-pressure or a statement of some antecedent illness as typhoid fever or pneumonia. These cases present nothing peculiar in their symptomatology, but should be carefully studied to ascertain the state of the vessels and heart muscle. Pulmonary oedema occasionally occurs in these patients.

The prognosis and, to a certain extent, the treatment depend upon the degree of damage sustained by the myocardium. This may lead to dilatation during life and consequent reflux through the mitral orifice. Instances of aortic insufficiency, of the kind now considered, are probably always secondary to syphilitic mesaortitis and not endocarditis. They may be quite appropriately regarded as cases of cardiac lues, yet their development is so insidious that recognition of the leak generally takes place after its complete establishment, and compensating hypertrophy has occurred. The myocardium may be found extensively degenerated.

Symptoms in these cases of pseudovalvular lesions are of the kind seen in failing hearts from whatever cause, but there are generally clinical data pointing to degenerative changes in the arteries, kidneys, and liver which assist in the recognition of vascular and myocardial decay as the fundamental condition. Such cases are extremely common among negroes, in whom they are probably of syphilitic origin.

Symptoms of the Fatty Heart.—There are undoubtedly cases of fatty overgrowth and infiltration which deserve the term *fatty heart* or *cor adiposum*, but it is an error to suppose that all obese individuals have

this kind of heart. It is likewise erroneous to infer that corpulent persons exhibiting signs of myocardial incompetence necessarily have fatty hearts. Furthermore, a heart that is enveloped in a thick layer of adipose tissue may be capable of performing its functions without evincing special weakness. These considerations render the term fatty heart objectionable, from a clinical standpoint. It would be far more in accordance with facts to adopt the term, *myocardial incompetence of the obese*.

The symptoms in this class are not peculiar, but are essentially those of cardiac inadequacy from other causes. When they arise it is usually in consequence of the heart's inability longer to endure the heavy strain imposed upon it by the obesity. Not only is the work of the organ magnified by the individual's weight, but the new vascular areas put additional burden on it. The heart has to do an extra amount of work commensurate with the degree of obesity. Some corpulent individuals, moreover, are anemic and the myocardium is inadequately nourished. This is one reason why some fat persons develop symptoms of cardiac incompetence at a comparatively early age.

The fat and anemic are in danger of overtaxing their hearts by unusual exertion, but, warned by their shortness of breath, rarely commit acts which seriously overstrain their heart walls. The fat and muscular, on the other hand, often subject their hearts to enormous strain and consequently form the class in which myocardial insufficiency is the more frequent. If the arteries are stiff, or if the blood-pressure has been high for many years in consequence of nephritis or other conditions not yet fully understood, the myocardium may be in a state of degeneration and hypertrophy. In such a case the condition is in reality a chronic myocarditis, not a fatty heart.

In a minority of cases the heart is neither fatty nor degenerated; it is simply inadequate because of the disproportion between its potential strength and the burden it has to carry. The organ has hypertrophied to its limit and then, being unable to hypertrophy further, it dilates. This is the first step and now distinctive symptoms appear.

Breathlessness on exertion is so usual in corpulent individuals that it is lightly regarded by them. Now, however, myocardial incompetence causes them to puff and blow in an unusual way and upon relatively slight exertion. Dyspnoea is now fully established and in some instances may be fairly constant. From this time on to the end it remains a marked feature.

The *pulse* is increased in frequency and regular or irregular as the case may determine. The blood-pressure may be augmented in the beginning, but tends to fall with progress of the inadequacy. In cases in which chronic myocarditis, secondary to renal disease does not coexist, the tension of the pulse may not be noticeably raised even with subjective symptoms.

Examination of the precordium is generally unsatisfactory. The cardiac impulse is not perceptible on account of the fat, and for the same reason it is difficult to obtain definite data by percussion. Auscultatory percussion may enable one to obtain a fairly reliable outline of the heart's area. Upon auscultation the sounds are apt to be distant and feeble,

and murmurs are generally wanting. Careful attention may detect special feebleness of the first tone at the apex, and accentuation of the pulmonic or aortic second sound. After the patient has been required to hop about the room, or to ascend a flight of stairs, a soft blowing murmur may develop in the mitral area. This sign, which is so commonly elicited in cases of myocardial insufficiency, is exceedingly important, since it indicates dilatation of the auriculo-ventricular ring occasioned by exertion. The roentgen-ray is usually necessary for determination of the size of the heart, and the degree of dilatation.

As a rule, fat people rarely exhibit as marked evidence of turgescence of the superficial vessels as do thin individuals. Indeed, capillary stasis may only give them a ruddy or plethoric appearance which may be mistaken for the hue of health. It may quite disguise the anemia actually present. The abdominal corpulence also prevents palpation of the liver, and hence stasis in this organ may not be detected. Puffiness of the ankles may be present in the beginning, and, as circulatory activity decreases may at length merge into actual oedema. The urine may present the changes of renal stasis or nephritis. The clinical picture is that of more or less extreme heart failure. The background of the picture is ever the same; it is only the details and coloring which are different, and these are determined largely by the degree of obesity.

Diagnosis. — Acute Myocarditis.—Not only is this a matter of difficulty and often of uncertainty, but the physician must endeavor to decide which form is present. He should never lose sight of the possibility of acute myocarditis in the course of infectious diseases, *e. g.*, pneumonia, influenza and diphtheria. Instability of the pulse, marked pallor and vomiting, restlessness or listlessness and apathy, are symptoms which should arouse suspicion of acute myocarditis. If, in addition, the heart becomes dilated and the tones feeble, there is good reason for assuming parenchymatous degeneration of the myocardium. A soft, systolic murmur often develops which, confined to the vicinity of the apex and accompanying but not replacing the first sound, is thought to indicate endocarditis. Such a murmur may, however, in many cases be caused by relaxation of the ventricular muscle, in consequence of which the mitral valve is not accurately closed. It is, therefore, the murmur of muscular mitral insufficiency, and in suspected cases affords corroborative testimony of the existence of some degree of myocarditis.

Interstitial, *i. e.*, suppurative myocarditis, may be suspected in the course of pyemia or puerperal sepsis if the clinical picture resembles that of malignant endocarditis with embolic phenomena, yet without distinct signs of valvulitis. In this as well as in the parenchymatous form, however, the diagnosis will generally be by inference and can rarely be absolute. In any case the probabilities are in favor of the parenchymatous rather than the interstitial variety.

Chronic Myocarditis.—The diagnosis of this affection may or may not be difficult in accordance with the extent and character of the changes in the heart and arteries, and the data furnished by the patients' history and symptoms. Cases may be divided into two main groups, as follows: (1) Those in which the symptoms and clinical findings leave no reasonable

doubt of their real nature, and (2) those which present equivocal evidence of arterial and cardiac disease, yet are at a time of life that renders probable the existence of degenerative changes. The former group interests the physician as a clinician and therapist, while the latter concerns him as a diagnostician and life-insurance examiner.

1. In this division of cases age is important, since if symptoms of heart disease develop in a person who has passed the prime of life, it is a fair assumption until proved otherwise that disease of the heart muscle is responsible. This is greatly strengthened by the failure to discover, in the history or physical signs, evidence of a lesion caused by endocarditis or pericarditis. If in addition the accessible arteries are sclerotic and the urine shows the changes of chronic nephritis, or if in the absence of demonstrable changes in the vessels or kidneys, the blood-pressure is abnormally and persistently high, there is good ground for believing that the myocardium is seriously degenerated. If the area of dulness is increased transversely, if the first sound at the apex is valvular and feeble or impure, perhaps accompanied by a circumscribed soft murmur, and if the aortic second tone is clanging, especially if in addition there is a distinct systolic murmur with or without dilatation of the aorta, then the diagnosis of chronic myocarditis may confidently be made.

On the other hand, it must be borne in mind that serious myocardial incompetence may exist with but few physical signs. The area of deep cardiac dulness may be but slightly increased and the sounds may be clear, presenting no other change than enfeeblement of the first and accentuation of the second sound in the mitral or aortic areas or both. Nevertheless such inconspicuous modifications taken in connection with age and subjective symptoms may furnish just the evidence required. Should the physician still be in doubt, the effect of brisk exercise on blood-pressure and pulse-rate is likely to settle the question. A healthy heart responds to brisk exercise not alone by acceleration of the pulse, but also by increase of systolic blood-pressure which remains raised over its original figures after the pulse has returned to its former rate. The pressure may then continue to rise or after a decline may again show an increase known as the secondary rise. In cases of incompetent myocardium the blood-pressure according to the degree of inadequacy may first rise but slightly and then fall rapidly to or below its original level, and before the pulse regains its former rate, or it may fail of any increase at all, but instead show a decline. Accordingly if a middle-aged person gives this blood-pressure evidence of myocardial incompetence, together with some of the data obtained by physical examination, it is a fair assumption that degeneration is present.

As a matter of fact the recognition of myocardial inadequacy is rarely difficult. The real problem to be solved is the underlying state of the heart muscle. Therefore when cardiac symptoms occur in a person under forty-five without valvular disease the real pathology of the case must be determined by close attention to the previous history as well as accurate investigation of the physical findings. The history of syphilis, of the abuse of alcohol, of gout, chronic plumbism or of severe infections strengthens greatly the probability of myocardial degeneration. If in

addition the blood-pressure is persistently too high or too low, or if the urinary findings indicate beginning renal change, or if anginoid pains are complained of, the case had better be regarded as serious rather than dismissed with the assurance that nothing is the matter.

2. Diagnosis in this class of cases is often very difficult. Subjective symptoms of myocardial failure are wanting or so inconspicuous as to escape notice. Moreover, the individual may present the appearance of perfect health and may not have reached an age that in itself suggests the possibility of degenerative change. It is just this type of person that comes up for life insurance and taxes the skill and judgment of the examiner to the utmost. As a fundamental step there should be a minute and rigid inquiry into the history, and attention must be paid to such illnesses and habits as may be of etiological importance.

Undue frequency of the pulse at the time of examination may result from apprehension or nervousness and not indicate heart weakness. Its real significance should be determined through repeated examinations or by studying the effect of posture. In the dorsal decubitus the pulse-rate should fall from 7 to 15 beats from that in the standing position, while when myocardial incompetence is present the rate in the recumbent posture may not fall. Should this test prove inconclusive, then the effect of brisk exercise on blood-pressure should be ascertained. Auscultation of the heart immediately succeeding hopping often assists in diagnosis, since if the myocardium is not equal to the effort it may be evinced by a soft systolic murmur at the apex indicative of slight dilatation and muscular mitral insufficiency.

Examination of the heart before exercise in these latent cases, as they may be termed, may or may not yield definite information. In some instances the cardiac dulness is plainly increased and the tones present some easily recognizable deviation from normal, such as feebleness of the first and undue intensification of the second sound, especially in the aortic area, where it may be quite metallic or clanging. Or there may be a systolic bruit of greater or less distinctness in the second right interspace which together with accentuation of the second tone suggests sclerosis of the aorta. Should the physician not be able to ascertain the size and shape of the heart by percussion, he should have recourse to a skiagraph and perhaps an electrocardiographic tracing. Yet in many cases the estimation of the blood-pressure will assist materially in determining the area of cardiac dulness, since an abnormally and persistently high pressure renders probable the existence of hypertrophy, and hypertrophy of the heart in a person of middle age may be regarded as synonymous with degeneration even though the potential integrity of the myocardium may not yet have suffered appreciably. Other corroborative testimony may be found in the state of the accessible arteries, in changes in the urine, and in evidences of visceral congestion.

In still doubtful cases, the electrocardiograph is likely to supply corroborative evidence of myocardial change, even in the absence of marked symptoms. Willius has shown that when the *R*-wave shows notching in all three leads it signifies arteritis of the septal arteries, a very grave prognostic condition.

It is well to say a few words concerning the recognition of myocardial incompetence in *women*. In them percussion of the heart is often impossible because of the mammary development, and yet there may be certain symptoms which make myocarditis highly probable. Under these circumstances valuable information may be obtained by careful palpation of the heart's impulse. It will often be perceived that the impulse is diffuse and extends too far to the left. Upon auscultation the first sound at the apex is not clear and strong, but valvular, or actually impure, and the aortic second is accented. In other instances it is the pulmonic second that is intensified. If in addition the blood-pressure is too high, and the woman suffers from greater breathlessness on exertion than should be the case in relation to weight or anemia, and if she be leading a strenuous social, domestic, or club life, the assumption is tolerably safe of chronic myocardial weakness, and if the age be fifty or thereabout this weakness probably rests upon a basis of chronic myocarditis.

Fatty Heart.—The existence of fatty overgrowth and infiltration to an extent occasioning myocardial incapacity must be a matter of inference rather than clinical demonstration. In the majority of fat persons who present cardiac symptoms the most we can do is to diagnose the incompetence. If the individual is very fat and at the same time anemic, is too young to warrant the assumption of cardiovascular and renal degeneration, and accordingly fails to furnish clinical proof of such myocardial changes, we may recognize heart strain as probable without degeneration. The case may then be said to come within the category of the myocardial incompetence of the obese. As a matter of practical interest it is not necessary to know whether the heart is actually fatty or not; it is overpowered by the general obesity, and this of itself forms a sufficiently serious condition.

Prognosis.—This is necessarily grave, since whatever impairs the structural integrity of the heart muscle is likely to limit its potential capacity. The heart is, however, a marvellous organ, whose possibilities for compensatory adjustment to altered conditions enable it to perform its function in a way that is truly astonishing. Accordingly it may be performing its work with but slight evidence of anything being wrong, while all the time a process of degeneration is going on.

Acute parenchymatous myocarditis may be recovered from, when not extensive, but the possibility of sudden death should always be borne in mind, especially during the course of diphtheria and even after convalescence. On this account a child should be kept under close observation, both when at play and at rest, for the detection of slight signs of incompetence. The *interstitial form* of acute myocarditis is probably always fatal, unless it be very circumscribed, which is not unusual.

Chronic myocarditis also carries with it the liability to sudden and unexpected death, and since we possess no means of determining the seat and extent of dangerous lesions, we must always regard as uncertain the life prospect in any individual with myocardial degeneration. Nevertheless, if hypertrophy predominates and symptoms of inadequacy cannot be discovered, we may hope that the potential integrity is still such

as will preserve the heart from incompetence so long as it is not too greatly overtaxed. When signs of incompetence once appear, prognosis becomes very serious and must be reckoned by the degree of insufficiency manifested, or by the response shown to proper treatment.

Persistent arrhythmia is generally held to be of worse import than is regularity even with tachycardia when this latter is not extreme, and yet one should look with apprehension on an habitually accelerated though regular pulse. Although irregular hearts may endure for years without distressing symptoms, still they always carry with them the possibility of sudden disaster. On the other hand, occasional irregularity of the pulse is not of itself a symptom of myocardial disease. Its cause must be sought elsewhere than in the heart itself. Degeneration of the left ventricle is more serious than degeneration of the auricles, and yet it is in the latter condition that arrhythmia is so common; while extensive fatty change in the wall of the ventricle is compatible with perfect regularity of action. When polygraph or electrocardiograph tracings show a persistent arrhythmia due to auricular fibrillation or interference with stimulus conduction to the ventricle, or when digitalis skilfully administered fails to correct the irregularity, the prognosis may be considered grave.

Angina pectoris is of evil prognosis, since, in the majority of cases, there is more or less atheroma of the aorta and interference with coronary circulation. This condition always carries with it the possibility of sudden death. The prognosis in myocardial incompetence, associated with chronic nephritis, is likewise very bad. The heart muscle may be assisted in doing its work for a time after the initial manifestations but when the break again occurs the mischief is likely to be irreparable. The development of alternation of the pulse or of gallop rhythm always, in the writer's experience, has portended a not very remote termination in death. This rhythm may persist for months, but it indicates a degree of strain of the ventricular wall to which it must inevitably yield in time. A heart weakened by chronic myocarditis may be capable of performing its functions, fairly well, so long as some extra burden is not imposed. Any illness may prove the last straw. This is particularly true of acute infections.

Fatty heart, or the cardiac incompetence of the obese, is extremely serious when pronounced since it is rarely recovered from. The more corpulent the individual the worse the prognosis, since it is hardly likely that the obesity can be materially reduced without endangering the nutrition of the heart muscle.

Treatment.—Preventive.—The establishment of so-called heart clinics in many cities has as its aim not only the prevention of heart disease, so far as that is humanly possible, but also education as to the means necessary to preserve the functional integrity of the already damaged heart. In like manner the private practitioner may well endeavor to spread a knowledge of the measures essential to the preservation of myocardial integrity. He should not wait until signs of structural injury declare themselves but in every case of illness, as tonsillitis, rheumatic or typhoid fever, influenza, etc., should address his efforts to safeguarding the heart

so far as possible against the development of incompetence after convalescence from the acute infection.

It is not always easy to detect the initial symptoms of acute parenchymatous myocarditis, but the possibility of its occurrence should always be borne in mind. It is better to err on the side of overcaution than of the assumption that all is right. Accordingly the child recovering from scarlet fever, rheumatic fever or what not should be given a rest period of weeks or perchance months if the heart action remain too rapid or a murmur persist.

The adult should without being unduly alarmed be told of the possibility of his myocardium having sustained some injury and of the harm likely to ensue if he subjects his heart to undue strain. He should be warned against rushing back into a strenuous business life, hurried walking and all other influences calculated to accelerate cardiac action unreasonably or in any way put undue strain upon the organ. A proper amount of rest is the best means for prevention of heart failure in these cases. Drugs may not be necessary but should breathlessness or palpitation out of proportion to the effort responsible indicate a weakened cardiac reserve, digitalis or one of its congeners may very properly be administered, the physician at the same time keeping the individual under observation. "An ounce of prevention is worth a pound of cure."

The foregoing outline of management applicable to cases of myocardial injury from acute parenchymatous change holds with equal force to persons with chronic myocarditis. The majority of people who have reached adult age and passed through one or more serious illnesses probably have heart muscles that examined postmortem would show areas of degeneration or previous inflammation. Although unconscious of symptoms of cardiac failure they are nevertheless potential candidates for disability. It is surprising how many such individuals live to old age without serious impairment of heart function. When however an individual in this category is found to present myocardial and arterial changes that may be classed as degenerative the rules laid down for prevention of lessened cardiac reserve should be impressed upon him. The writer recalls more than one man beyond middle age who, had he been informed of the danger from mountain climbing, could have been spared the heart strain which led to his subsequent breakdown from dilatation of his degenerated but until then functionally intact heart. Such persons should be warned of the danger in excess of any kind whether of work, sports, dancing, eating, drinking, smoking, etc. This applies with special force to persons having abnormally high blood-pressure with or without pronounced hypertrophy of the left heart.

The Treatment of Threatened or Actual Myocardial Incompetence.—*Rest* either partial or complete from whatever may be overtaking the weakened heart is the measure of greatest importance. The degree of incompetence must determine the completeness of physical rest to be enforced. In most instances digitalis or strophanthus is indicated in doses that accomplish the end desired. The intravenous administration of these remedies has come greatly into vogue of late and often brings about most gratifying

results. Given in this way or by mouth the effect should be carefully watched. Many therapeutists are in the habit of speedily digitalizing the patient and then withdrawing the drug because they believe its slow elimination will maintain its effect for a considerable time.

That rapid digitalization is not devoid of danger in myocardial incompetence is proved by the occasional report of sudden death. To the writer it seems safer and equally efficient to follow the habit of bringing the heart more slowly under the influence of the drug and then maintain its influence by carefully determined doses administered usually by mouth and continued at not too short intervals so long as required.

Although digitalis, if used with discretion may benefit some persons with abnormally high blood-pressure, in particular high diastolic pressure, still the best results are generally seen in patients with heart failure and diminished pulse pressure, for when the systolic is reduced without corresponding lowering of diastolic pressure the myocardium is plainly unequal to the labor of maintaining adequate arterial circulation.

The patients just referred to commonly show signs of more or less venous stasis with dyspnoea out of proportion to the effort occasioning it. In most instances hypostatic rales develop at the bases of the lungs with hepatic congestion and beginning anasarca. In such patients it may not be safe or effective to force the heart by digitalis alone to reestablish equilibrium between the venous and arterial streams. Other measures should be used, such as hydrogogue cathartics, a restricted intake of fluids and morphine or codeine sulphate subcutaneously to induce sleep and relieve distress. The writer is in the habit of placing such patients on milk in a daily amount nearly if not quite so small as the 27 ounces (810 cc.) familiarly known as the Karell diet. Such measures in many instances restore the heart to a fair degree of efficiency, when by slow steps the rigor of treatment may be lessened. But when this stage has been reached the admonitions respecting prevention must be impressed upon the patient. Even when the individual is discharged from hospital or his room he should be kept under observation lest he neglect his remedies or commit some indiscretion sure to bring on another and this time more serious breakdown.

Cases of Seriously High Blood-pressure.—It would seem that the proper management of such would be the reduction of the hypertension to spare the heart the strain of maintaining adequate arterial circulation, especially in the face of dangerously high diastolic pressure. Unquestionably this would meet the therapeutic indications but unfortunately is rarely possible owing to the atheroma already present in the arterial coats and our ignorance of the etiological factors that have led to the hypertension. Furthermore these patients rarely come under observation until the increased blood-pressure has persisted for years or sufficiently long to call the notice of the patient or examiner to the pathological change.

The most that can be hoped for as a rule is to protect the circulatory apparatus from more serious consequences and prevent, if possible, the blood-pressure from becoming still higher. To accomplish this the habits as regards diet, work, elimination, etc., must be carefully overhauled. It is of utmost importance to inform the individual that his cardiac

reserve is threatened in proportion to the degree of hypertension. The kidneys also are generally involved in the pathological change even though the urine and blood chemistry may not show much retention of urea and protein nitrogen and only a trace of albumin may be detected on urinalysis. The total intake of calories must be restricted within physiological limits depending on the amount of exercise taken. This applies particularly to the nitrogenous constituents, while at the same time articles of diet should be ordered that can be easily digested and will not cause annoying fermentation in the stomach or intestines.

It is advisable to pay specific attention to the intestinal excretion since, no matter if there be a regular daily stool, accumulation within the colon is likely to create subjective discomfort and augment pressure within the abdominal and hence general arterial system. It is a good plan to order a brisk purge once in four weeks, especially after a more than ordinarily hearty meal.

It would seem as if vasodilators, such as one of the nitrites, should be of value in lowering blood-pressure, but their action is so evanescent that except to meet certain conditions vasodilators are of slight benefit. When the indication for their use arises the patient or nurse should be explicitly instructed when and in what dose the drug is to be taken. Now and then the subject of hypertension may be annoyed or perchance alarmed by palpitation or rapid action of his heart. Such symptoms may usually be allayed by the administration of sodium nitrite in 1 gr. (0.065 gm.) doses several times a day with 15 to 20 minims (1 to 1.5 cc.) of the official 10 per cent. tincture of aconite root, or instead of the nitrite, bromide of strontium may quiet the patient and augment the action of the aconite.

Probably no one therapeutic agent is more often prescribed in cases of hypertension with thickened arterial coats than an iodide, but candor compels the admission that excepting in persons with a syphilitic history no distinct lessening of blood-pressure has been secured, although more or less subjective sense of benefit may warrant this measure. Since calcium is a tonic to the heart muscle while potassium is not, the writer has prescribed iodide of calcium rather than the potassium salt.

Venesection may be a life-saving procedure when blood-pressure becomes so high as to threaten cerebral hemorrhage or acute cardiac dilatation. It may very appropriately be combined with rest in bed and the restriction of the diet to a quart of milk daily or fruit juices alone until the dangerous symptoms have passed.

As regards the treatment of persons who suffer from Heberden's angina pectoris what has been said regarding the general management of myocardial degeneration applies with special force. As a rule all we can do is to allay the pain by the prompt administration of amyl nitrite or nitroglycerine, but in those instances falling under the head of Allbutt's angina due to atheroma and possible dilatation of the suprasigmoid portion of the aorta surprising benefit sometimes follows the prolonged taking of benzyl benzoate in milk or cream in doses of 40 minims (2.6 cc.) four times daily.

NEW GROWTHS AND PARASITES IN THE MYOCARDIUM

1. **Syphilis.**—**Etiology.**—The *Treponema pallidum* is believed to display a predilection for the cardiovascular system. Although cardiac lues is considered a late manifestation, declaring itself years after the initial sore, still cases have been reported of death from rupture of an aortic aneurism or of an aneurismal dilatation of one of the sinuses of Valsalva within a few months after the chancre. Although cardiac syphilis may be congenital it occurs most often in adults. It is said to exist more often in the male sex, although females are by no means exempt.

Morbid Anatomy.—This disease may give rise to changes of a chronic nature in any of the cardiac structures, but the endocardium is the least likely to be affected. In the *aorta* it appears as a mesaortitis which leads to aneurism or to aortic regurgitation with but moderate dilatation of the vessel. In such instances the aortic valves are quite likely to display changes due to cellular infiltration and thickening while the adjacent endocardium may show slight degenerative change of a yellowish color. In the heart wall the disease is said to appear generally either as a sclerotic process or as gummata. Warthin has demonstrated areas of fatty degeneration in which the spirochete was identified. He believes that degeneration of the myocardium is more often syphilitic than has been thought hitherto. Fibrous thickening of the endocardium or pericardium may be associated with the process in the myocardium. The sclerotic form of cardiac lues is said to be more frequent than gummata and affects chiefly the wall of the left ventricle, appearing as circumscribed patches of fibrosis.

The *coronary arteries* generally show obliterative endarteritis, that is, cellular infiltration and thickening of the subendothelial layers and consequent obliteration of the lumen. Osler states that gummatous periarteritis may affect the coronaries as well as the arteries of the brain, although less frequently. This is the only form of arteritis which can be regarded as specific. Should the endarteritis obliterans of Heubner be found in association with syphilitic lesions in other parts of the heart, or other organs, its luetic nature may be regarded as assured.

Gummata in the heart wall are comparatively rare. The tumors may be recent or old and single or multiple; the gumma appears as a soft, grayish mass of variable size surrounded by a capsule of fibrous tissue. Old gummata are dry, caseous, and yellowish-white. The pericardium overlying the gumma is usually seen to be thickened but seldom adherent. There may also be outgrowths upon the valves, as reported by Janeway and others, in association with gummata in the myocardium.

Symptoms.—Except in cases in which mesaortitis has led to aneurism or aortic regurgitation, heart syphilis is far less often recognized clinically than postmortem. The explanation lies in the fact that it quite often remains entirely latent. Even when symptoms are produced, they do not present features that may be considered characteristic or distinctive. *Tachycardia* and *arrhythmia* have been emphasized by Semmola. They may occur alone or together, but to be significant must be independent of any other discoverable cause, as dilatation or valvular disease. There

have been a number of cases of bradycardia with convulsive seizures and other features of the Stokes-Adams syndrome in which after death a gumma was found involving the bundle of His. *Precordial* pain of an indescribable or dull character, or of the nature of a vague distress rather than actual pain, has been described. *Angina pectoris* has been noted, and in a person under forty-five years of age, is very suggestive of coronary sclerosis or mesaortitis with or without dilatation due to syphilis.

Examination of the heart may or may not reveal signs of disease. There may be appreciable enlargement, or on careful percussion its area of dullness may appear entirely normal. This latter is one of the points on which Runeberg lays stress in connection with suspicious symptoms. Not infrequently the tones are clear but there may be a muffling or tonelessness of the first sound at the apex. Since lues generally affects the arch of the aorta as well as the heart muscle, an aortic systolic murmur may be the only positive abnormal finding. The roentgen-ray, if not percussion, is likely to reveal widening of the aorta.

Diagnosis.—Except in cases characterized by signs of involvement of aorta and valves this must be inferential or problematical. The occurrence of the symptoms mentioned in an individual with evidence of syphilis in other parts renders the diagnosis reasonably certain. In most cases the diagnosis must be established by history and exclusion rather than direct evidence. Tachycardia and arrhythmia, without obvious signs of disease in heart or bloodvessels, and to account for which no disturbing factors can be discovered in other organs is, according to Semmola, good and sufficient ground for antisypilitic medication. Angina pectoris in a man under forty-five may also be considered of luetic origin, provided no other satisfactory cause can be determined. The Wassermann reaction is of great value, and in suspected or doubtful cases should always be done.

Prognosis.—This may be said to be good, provided treatment is instituted before the development of irremovable changes. When unrecognized and, therefore, untreated, it is likely to lead to a fatal termination in the course of time. Extensive coronary sclerosis or aortic aneurism is very likely to terminate in sudden death. The development of anginal seizures is of very grave significance and renders the individual wholly uncertain of life.

Treatment.—This must be antisypilitic (arsphenamine and mercury) in the hope of arresting or removing the changes. To be efficient, the remedies should be pushed to the limit of toleration and ought to be continued for a long time after the cessation of symptoms. In particular the heart should be spared from strain during the course of specific treatment and the individual's general health receive close attention. It is best to administer mercury and arsphenamine periodically over a term of years.

2. **Tuberculosis.**—Tubercles may occur in the myocardium with tuberculous pericarditis and in general miliary tuberculosis.

Morbid Anatomy.—This possesses greater pathological than clinical interest. Miliary nodules scattered through the myocardium, caseous masses or a diffuse sclerotic process may occur. The tubercles are said

to be discovered especially in the sulci along the line of the vessels. Caseous tubercles are exceedingly rare, while the sclerosis of tuberculous origin presents no features that distinguish it from the same process of other causation.

Symptoms.—If such are produced they are obscured by those of the tuberculous infection in general. The invasion of the heart is said to occur chiefly in acute cases, and hence undue rapidity or feebleness of the heart's action is likely to be attributed to the asthenia and pyrexia of the primary affection.

Diagnosis.—This can be made with certainty only postmortem.

Prognosis.—This is in reality that of the primary infection. It probably exerts but little influence on the course of the malady.

Treatment.—This includes the administration of digitalis, etc., if cardiac asthenia becomes pronounced.

3. **Blastomycosis.**—Another of the rarities of medicine is the dissemination of blastomycotic granules in the myocardium. They occur as a part of generalized blastomycosis. In the case recorded by Clary¹ the fungi were discovered in the myocardium at postmortem. The heart weighed 180 gm. and scattered through the heart walls were miliary nodules resembling those of tuberculosis. The clinical picture in this case was that of chronic nephritis. Blastomycosis of the heart possesses no clinical interest, since it is secondary and but a part of the generalized disease, and can only be surmised, not diagnosed, during life. It is doubtful if it materially influences the prognosis, which, to judge from reports, is absolutely hopeless.

4. **Actinomycosis.**—Hektoen states that actinomycosis of the myocardium is more frequent than either syphilis or tuberculosis in this situation. Perhaps the results of the Wassermann test and Warthin's contributions to cardiac syphilis, made since the foregoing statement by Hektoen, would modify the latter's declaration. Any portion of the circulatory system may be attacked, but the endocardium appears to be involved rather less frequently than the pericardium or heart wall, and then in consequence of encroachment of a myocardial process upon the cavities of the organ.

Etiology.—The invasion of the heart may be by direct extension or by the blood stream. Involvement through the lymphatics has not been demonstrated. The metastatic form is stated to be the more common, which is not surprising when one understands the frequency with which actinomycotic masses are found projecting into the interior of the veins in various parts. When the process has extended from the lungs or other adjacent structures, there are generally dense fibrous adhesions binding together the various tissues.

Morbid Anatomy.—Actinomycotic granules within the myocardium vary much in number and size. They have been found in all portions, including the auricles and papillary muscles. These foci are more often metastatic in origin and hence may be either single or multiple. Their size is also not constant, but the majority range between 1 and 4 cm.

¹ *Transactions of the Chicago Pathological Society*, 1904, vol. 6.

in the greatest diameter. The largest mass on record is that of Ponfick, which was a yellowish nodular mass, of the size of an apple, situated in the wall of the right heart at the level of the auriculo-ventricular opening.

Foci of myocardial actinomycosis are very apt to set up either circumscribed or diffuse pericarditis, which may be exudative or fibrous. The exudate may be fibrinous or serofibrinous, and in some instances purulent. Not infrequently this exudate is found to contain the characteristic sulphur granules of the actinomycotic fungi.

Symptoms.—These are apt to be obscured by those of the process in the lungs or other parts. They will depend upon the character of the changes that have taken place in the pericardium or elsewhere.

Diagnosis.—This can only be surmised, not definitely determined. The appearance of cardiac incompetence or signs of pericarditis, in a person suffering from actinomycosis, would render probable the involvement of the cardiac structures and, therefore, of the heart walls.

Prognosis.—This is hopeless.

5. New Growths.—These are both relatively and absolutely very rare in the heart. They may be of any kind, although some occur more often than others. The variety of heart tumors is shown by Berthenson's figures, who, out of 30 instances found 9 of sarcoma, 7 of myoma, 6 of fibroma, 2 of gumma, and 3 each of carcinoma and cystic tumors. Of these the cardiac cavities were invaded in 22 cases (Whittaker) as follows: right auricle 7 times, right ventricle 3 times, left auricle 7 times, and left ventricle 5 times. Lipoma and myxoma have also been found, but are still more uncommon than the forms already mentioned.

Although too many malignant neoplasms have been reported to make them a clinical curiosity, still their absolute infrequency is shown by the fact that up to 1893, Tedeschi was able to find only about 80 cases in the literature. To these he added 3 of his own, and as others have been recorded since then, it may be safely stated that the total number to date will fall not far short of 100. Carcinoma is more frequent than sarcoma, and yet the relative rarity of cancer of the heart is shown by the following figures: Koehler found but 6 instances among 9118 autopsies, Fanchon 6 in 8189 autopsies, Willigk 9 of the heart and 7 of the pericardium in 4547 autopsies. The infrequency of cardiac cancer may be further judged by the fact that Willigk's 16 instances occurred among 477 cases of the disease in general. When we consider primary and secondary cancer of the heart, primary cancer is by far the less frequent.

Etiology.—Malignant growths in the myocardium are very rarely primary. The neoplasm is most commonly secondary to disease of the mediastinum or lung, but may be metastatic from distant parts. In some instances the growth invades the heart by direct extension. The disease may occur at any age, even in childhood, but is of course most frequent in middle age.

Pathology.—Malignant neoplasms, whether carcinoma or sarcoma, are usually secondary to malignant disease of neighboring or distant parts. They may occur in the heart as either a single growth or as multiple nodules, more often the latter. The disease seems to be situated rather more commonly in the right side of the heart, especially when it

is metastatic. In not a few instances the growths invade both the pericardium and myocardium, and it is often difficult to decide in which of these two situations the disease is primary. Multiple nodules throughout the heart cause great enlargement of the organ, and the pericardium may be filled with a bloody exudate in consequence of the invasion of the sac. The tumor may obstruct the orifice near which it is situated, and, if the mass projects into the cavity, the endocardium overlying it may be eroded. As the cancer is most often of the colloid variety it is likely to give rise to metastases, and the pulmonary artery may be occupied by carcinomatous emboli, as in Osler's case.

Symptoms.—There is nothing characteristic. There may be evidences of heart weakness, the pulse may be accelerated and irregular; but as the location in the heart is usually secondary to disease of other structures, these symptoms may be attributed equally well to that fact. Precordial pain has been noted, and in such cases is probably to be referred to pericardial involvement. Distention of the pericardium, with sanguineous fluid, is shown by the usual signs of pericardial exudate.

Diagnosis.—This is either impossible or a matter of good fortune. It is extremely doubtful if primary cancer of the heart can every be diagnosed with certainty, and except in unusually favorable cases even the secondary form must be inferred rather than determined with positiveness. Involvement of the myocardium may be surmised upon the development of cardiac symptoms, that are more severe or of another character than can be readily explained by mere weakness on the part of the patient; likewise, if precordial dulness becomes so increased as to point to distention of the pericardium with fluid, or if signs be detected which indicate obstruction of an orifice or leakage of a valve.

Prognosis.—This is absolutely hopeless.

Treatment.—This is limited to the relief of symptoms and the sustaining of heart power.

6. **Echinococcus.**—This is very rare in the myocardium. Of 1862 cases of hydatids, in the united statistics of Davaine, Cobbold, Finsen, and Neisser, there were but 61 instances in which the heart and blood-vessels were the seat of the disease.

Etiology.—Echinococcus disease of the heart may be primary, but is usually secondary to hydatids in other parts. In either event the parasites are conveyed to the heart in the blood stream.

Pathology.—Echinococcus cyst of the heart may be either intramural or endocardial, and may vary in size from that of a bean to that of an orange. The number of the hydatids also varies much. There may be but a single cyst situated in the myocardium, or there may be many cysts occupying and completely filling a cavity. When in the interior of the heart the cysts may be loose or pedunculated.

Symptoms.—These depend upon the seat of the cysts, whether in the wall or a cavity of the heart. They cannot be predicated, therefore, and indeed are probably disguised by signs pertaining to the disease in other organs. The fact of sudden death from blocking of a pulmonary artery by cysts in Crowther's case should be kept in mind, as well as the possibility of pulmonary echinococcus from rupture of a primary

hydatid of the myocardium, as in Grulee's patient. Serious obstruction to the circulation may result from cysts in the interior of the heart.

Diagnosis.—This can only be inferred when, in an individual known to have echinococcus disease of the liver or other viscera, symptoms arise which point to possible implication of the heart.

Prognosis.—This depends largely upon the seat and subsequent history of the cyst. Its rupture may cause death, or be responsible for a secondary invasion of the lungs through which the life of the individual ultimately may be sacrificed. In most instances death is like to occur, either directly or indirectly, through the cardiac disease.

Treatment.—This must be purely symptomatic.

CHAPTER XVI

ACUTE ENDOCARDITIS

By JAMES B. HERRICK, M.D.

ACUTE endocarditis is described here as of two forms, simple and malignant. The rheumatic type is treated under the head of acute simple endocarditis. The malignant group is divided into an acute form and the important subacute form sometimes called chronic. Chronic endocarditis in a strict sense, a condition not clearly defined, often confused with degenerative sclerotic processes, recurrences of acute forms and with valvular defects, is not considered here. Syphilitic endocarditis is not included except to be casually mentioned.

Etiology.—Acute endocarditis is an acute inflammation of the lining membrane of the heart and its valves, the result of infection by micro-organisms. The ones most often found are the streptococcus (hemolyticus and viridans), pneumococcus and gonococcus but many others are occasionally met with. The streptococcus is the most frequent agent, and especially if we look upon it, or some closely related organism, as the cause of rheumatic fever and chorea, which cause such a large proportion—approximately 50 per cent. of the cases of acute endocarditis, particularly in children. The spirochete of syphilis may cause an endocarditis which though oftener subacute or chronic in character is at times acute. Acute syphilitic aortitis and aortic valvulitis are probably much more frequent than is generally believed; they easily escape detection.

Just what part toxic material plays in the production of acute endocarditis is questionable. Koeniger assigns to it a very important rôle. A. B. Wadsworth from observations made during experimental work with the pneumococcus in horses concluded that the toxin played an important part in the production of the acute endocarditis, preparing the soil for the bacterial growth. It may well be that in connection with microbic invasion of the body, the toxins are in a measure instrumental in producing the local lesions. Thus, as a terminal accompaniment of malignant tumors, diabetes, leukemia, or chronic nephritis, in which diseases there is no known microbe at work, a mild type of acute endocardial inflammation is sometimes seen. Similarly in long-standing cases of tuberculosis fresh, bead-like vegetations are found at times, paralleling the edges of the valves, in which vegetations no tubercle bacilli or other germs can be identified. It is thought by some that toxic influences may here be responsible.

Acute endocarditis is to be regarded as a *secondary* condition, there always being some other infectious process that may be looked upon as primary. Occasionally the disease is referred to as primary. This means, certainly in most instances, that the primary focus has escaped detection.

The primary infection is most frequently some specific disease like rheumatic fever, chorea, scarlet fever, gonorrhœa, epidemic meningitis, diphtheria, typhoid fever or pneumonia. There is a large group due to the ordinary pyogenic organisms. This includes cases in which the infection originates in wounds that are infected, in abrasions of the skin, furuncles and carbuncles. There may be breaks in the mucosa, as in the urethra when a sound has been violently passed. The stomach or bowel may be the seat of an ulcerative process which allows the entrance of germs. Much attention has been attracted to the mouth as the source in many cases. Pyorrhœa, suppuration about the roots of the teeth, infected tonsils and adenoids, are to be viewed with suspicion when other sources are not clearly at fault. Suppurative processes anywhere in the body may supply the germs that carried to the heart, if conditions are favorable, set up an acute inflammation. Osteomyelitis, a suppurating nasal sinus or middle ear, pyelitis, cystitis or an infected gall-bladder may be the source of the cardiac disease. In many cases the endocardium is but one of many localizations of the microorganisms, as is the case in rheumatic fever. In pyemia there may be associated acute pneumonia, nephritis, pleurisy, arthritis, etc.

Under the head of rheumatism may be grouped not only the typical cases, but diseases closely related clinically and probably etiologically such as chorea and some of the erythema and purpura group. Tonsillitis must in some instances be regarded as a manifestation of rheumatism.

It is generally believed that the endocardium becomes involved because bacteria in the blood-stream lodge on the lining membrane of the wall of the heart and especially upon the valve surface, and having once gained a footing work as they might in a joint or in the pleura to produce inflammation. This implantation theory, at least in its entirety, is not accepted by all. Some (Poynton, Rosenow, Koester) contend that though the valves are poor in bloodvessels, the bacteria may reach the valve by emboli, go out to the farthest point in the valve to which the vessel will carry it—or go into the lymph spaces—and there induce inflammation. This embolic view will be referred to more particularly when discussing malignant endocarditis.

Classification.—This is at present unsatisfactory. It is desirable to classify endocarditis according to the nature of the infecting agent, but this cannot always be done. Other classifications have been made, verrucose and ulcerative based on the anatomical lesion; benign or simple and malignant, septic or infective, based largely on the severity of the symptoms. No hard and fast line can be drawn between these two groups either pathologically or clinically. They are essentially much the same, bacterial in origin, toxic-infectious in character, with lesions often differing rather in degree than in essential nature. But in what may be regarded as typical cases, one shows a fairly uniform pathology and a tendency toward healing with disappearance of symptoms while the other reveals its malignant character in presenting characteristic tissue changes and being malignant in its constitutional manifestations, death being the usual result. Not a few cases, however, are of such a nature that they may well be placed in Libman's indeterminate group.

The classification of Libman has much to commend it. He makes five groups: rheumatic, syphilitic, acute bacterial, subacute bacterial, and indeterminate. In separating the rheumatic from the bacterial he does not mean to deny the possibility of the bacterial origin of rheumatic fever. He merely recognizes the fact that the cause has not been proved and that pathologically and clinically the rheumatic form of endocarditis has distinctive marks.

Without quibbling over the question of terminology—there is some argument in favor of each name employed—we shall use the terms simple and malignant and group our cases for description as nearly as possible under these two heads. One must not, however, in using the words simple and benign get the impression that this form is insignificant—far from it. In its end-results it is too often disastrous, as a large proportion of cases of chronic valvular lesion have their origin in it. Sir William Osler well said: “There is no benign or simple form. Endocarditis is always a serious lesion. . . . The so-called benign endocarditis kills in the long run a very much larger number of persons than the malignant form.”

ACUTE SIMPLE ENDOCARDITIS

Pathology.—Through the influence of the infectious-toxic agent an area of local necrosis is produced in the endocardium, oftenest in the valves of the left heart, although the tricuspid valve is by no means exempt. Thayer found it involved in 44 per cent. of 25 cases of rheumatic endocarditis. Libman notes an even higher percentage of tricuspid rheumatic cases. A reactive proliferation of the neighboring endothelium and the underlying connective tissue results, causing a little swelling which is capped by a layer of fibrin, with red and white blood corpuscles and blood platelets. This is the thrombo-endocarditis of many authors. At autopsy the causal microorganisms may or may not be found. At times those found are secondary invaders which have lodged in the thrombotic mass. When no organisms are found in smears or cultures it is believed by most that they have died out.

These bead-like or warty vegetations are on the line of closure of the valves, the auricular side of the bicuspid valves and the ventricular side of the semilunar valves. In long standing cases new vessels may work out toward, or even into, these excrescences. When healing occurs connective tissue and endothelial cells invade the vegetation with resulting scarring that often deforms the valve and interferes with its function.

It is not unusual for other parts of the heart to be involved as well as the endocardium. This is particularly true of rheumatic fever in which there is quite uniformly an acute myocarditis with the characteristic Aschoff bodies, and often a pericarditis. In rheumatic fever the vegetations seem to be larger than in most other forms of simple endocarditis, invade the underlying tissue more deeply and show a more marked tendency to initiate a chronic deforming process. There is justification for the use of the terms, rheumatic cardiopathy, rheumatic heart and rheumatic pancarditis. Chorea¹ is to be viewed as a cerebral manifestation

¹ Cf. Swift, Carey Coombs and others.

of the same rheumatic process that elsewhere produces polyarthritis, subcutaneous nodules and carditis.

Symptoms and Diagnosis.—In reality there are no distinctive symptoms by which acute endocarditis of this type may with certainty be recognized. Many cases are latent, especially in children, and it is only when, months or years afterward, a definite valvular lesion is discovered that it is known that during an acute illness an acute valvulitis had developed. The possibility—one is tempted to say the probability—of the existence of these masked cases should always be remembered in connection with rheumatic fever and chorea. Another difficulty lies in the fact that acute myocarditis may be largely or entirely responsible for the symptoms of cardiac involvement and it may not be possible to say whether there is valvular disease or not. The salient facts on which one attempts to base a diagnosis are the following:

(a) The existence of a *primary causal disease*—rheumatic fever, chorea, purpura, tonsillitis, pneumonia, puerperal sepsis, gonorrhoea, scarlet fever, etc. In this connection the milder manifestation of rheumatic fever and tonsillitis must not be too lightly regarded.

(b) Alteration in the heart's *rate and rhythm*. Generally the heart is more rapid than a subsiding rheumatic fever or a resolving pneumonia or a tonsillitis warrants. A rapid, irritable or irregular heart, when the fever has nearly or completely subsided after one of these infections, should arouse suspicion of cardiac involvement. Missed beats at the wrist, due to premature contractions, or the more serious bradycardia due to heart block may be due to myocardial with endocardial changes. Electrocardiographic examination, while rarely necessary, may be helpful in the recognition of the carditic process.

(c) The *heart tones* show impurity. If this impurity rises to the grade of a murmur and if this murmur be diastolic or presystolic, a valvular lesion is almost certainly present. While systolic murmurs may be indicative of involvement of the valves, they do not give definite assurance of such a lesion as they may be caused by a weakened musculature with intact valves. There is, perhaps, a present-day tendency to pass over systolic apical murmurs too lightly, to regard them as accidental or inconsequential, "as it is the muscle and not the valve that counts." While there is much justification for this attitude toward systolic murmurs in connection with chronic heart conditions, one must remember that in acute conditions they are only too often caused by a genuine valvular inflammation and are of serious import. In acute rheumatic fever particularly, the burden of proof should rest on the one who declares that systolic murmurs are not due to organic change. The assumption should be that they are organic.

At times a sharper ring to the pulmonic second tone may appear. Or the heart may show an enlargement proved by the altered location of the maximum impulse or by increase in the area of dulness. The heart tones may lack some of their normal intensity or the whole action may be weak. On the contrary, there may be an increased, almost pounding, beat of which the patient is conscious and which may be very annoying.

(d) *Subjective sensations* of weakness, malaise, etc., are sometimes described. There may be precordial oppression even amounting to definite pain, especially in the recurring endocarditis of old mitral or aortic disease. A coincident pericarditis may cause quite marked suffering.

(e) The *temperature* is variable. It may not rise above normal or it may be high. As a rule, however, there is a persistent, low fever—99° to 101°—after the subsidence of the manifestations of the primary disease. This should arouse suspicion and it is a good rule to follow, in a case of rheumatic fever, especially in a child, when the throat, joints and pleura seem free from evidence of inflammatory activity, and yet in whom there is a daily rise of temperature, even though slight, to regard such fever as due to an endocarditis that is still active. Fever is really the most important sign of this disease.

It must not be forgotten that under the influence of fever and toxemia the heart may be rapid and a systolic murmur may be heard, especially at the apex or in the pulmonary valve area and yet no valvular disease be present. This febrile heart, or toxic heart as Mackenzie called it, must always be considered and excluded before one decides that there is organic involvement of the heart. With the febrile heart, as the toxemia and fever disappear, there is a return to the normal rhythm and a disappearance of the systolic murmur. There are, moreover, no left-over subjective cardiac symptoms, unless the patient be a neurotic.

In rheumatic carditis the polymorphonuclear leukocytes are generally increased relatively and absolutely. There is a moderate grade of secondary anemia. Blood cultures are, as a rule, sterile. There is often a trace of albumin in the urine.

There is no clear-cut picture of acute simple endocarditis. It is only by the grouping of symptoms and signs and the elimination of other conditions that might cause them, that one may reach even a probable diagnosis. The question is often impossible to settle as to how much myocardial changes have to do with it all. Perhaps this is an advantage for this uncertainty should make the physician particularly careful in his predictions as to the immediate and remote outcome.

Prognosis.—So far as life is concerned simple endocarditis *per se* rarely causes death. Remotely, however, through later valvular defect, it may prove fatal. To these cases of acute rheumatic carditis one may aptly apply the old adage: "*In cauda venenum.*" The original disease, rheumatic fever, chorea, scarlet fever, pneumonia, etc., may cause death or the cause may be the accompanying myocarditis or pericarditis. Other complications of the primary disease, as pleurisy, bronchopneumonia or nephritis may lead to a fatal result. This implies that the function of the valves is seldom interfered with to such an extent as to be immediately of great consequence. In other words, death is not usually caused by interference with the mechanical function of the heart. There is, however, a type of the disease in which there seems to be a progressive and relentless weakening of the cardiac power in spite of all that can be accomplished by rest and other forms of treatment. It is seen oftenest in the rheumatic form in children. The fever may drag on for weeks, the heart

enlarges, its impulse is forcible and heaving, murmurs are persistent, dyspnœa, cyanosis and dropsy become marked and the sufferer succumbs, largely to the disturbance of the propulsive power of the heart. Death is pancarditic however, and not endocarditic alone.

The termination of acute simple endocarditis may be as follows:

1. Complete recovery with normal cardiac function restored.
2. Apparent recovery, yet later, evidence of a resulting valvular defect.
3. Myasthenia cordis, dilatation and death. This result is due more to myocardial and pericardial than to valvular disease.
4. Embolic complications, *e. g.*, in the brain, may be fatal. These are rare in the rheumatic forms.
5. Other infectious or visceral complications may occur such as pneumonia, pleurisy or nephritis.
6. Recurrences may take place or the disease may pass over into the malignant type. In old aortic and mitral lesions, especially the rheumatic forms, recurrences are not uncommon, both in adults and children. In some of these recurrences the disease may assume the malignant form.

Treatment.—The only treatment that can in any sense be regarded as specific is the treatment of the primary diseases. In these diseases proper treatment would, if given early, aid in preventing an acute endocarditis. All means employed to guard against infections are means, also, of guarding against a resulting endocarditis. Proper quarantine or protective inoculation against diphtheria, or scarlet fever and careful asepsis during a surgical or obstetrical procedure may prevent an endocarditis, as may the avoidance of gonorrhœa or its prompt and successful treatment. The same is true of syphilis.

Here we may stress the importance of careful attention to recurring infections of the throat and nose. Repeated attacks of tonsillitis or of inflammation in a chronically infected nasopharynx with adenoids may lead to inflammation in more distant parts as joints, nerves, kidneys or heart. Without being radical, one may urge the surgical treatment of infected tonsils and adenoids in children as a preventive measure. Even though endocarditis is already present surgery may not be too late to do good, for recurrences and recrudescences in acute endocarditis are common. Each new attack adds to the likelihood of increasing the valvular deformity and weakening the muscle by the accompanying myocarditis, or, in a recrudescence, of lighting up the malignant form of the disease. The *Streptococcus viridans*, which is so common a cause of the malignant form, is often found in infected tonsils and diseased teeth.¹

When there is a suspicion of cardiac involvement unusual precautions should be taken against allowing the patient to get out of bed too early. This applies with especial force to rheumatic fever. Injury to the valves

¹ Just how much is accomplished by tonsillectomy in preventing rheumatic fever and endocarditis or the recurrence of these conditions has not been definitely settled. Reliable statistics are not easily obtainable in studies of even a large series of cases of this character. Impressions are notoriously often deceptive. We find some observers strong in the belief that after tonsillectomy, rheumatic and endocarditic manifestations are materially lessened in frequency, while others are frankly skeptical as to resulting benefits. Further study is desirable.

and muscles may be lessened—perhaps avoided—if the rheumatic child is kept quiet for a long time.

How much good is accomplished in warding off or modifying acute rheumatic endocarditis by treatment with salicylates is problematical. Sodium salicylate, with bicarbonate of sodium or with alkalis such as potassium or sodium citrate or acetate, lessens the disagreeable manifestations of rheumatic fever—fever, pains, etc.—and possibly tends to cut short the disease. If there is this benefit, and I am inclined to think it is real and not imagined, there may be some service rendered in keeping down an acute endocarditis. The depressing effect of salicylate on the heart should not be forgotten. Especially when the pulse is very rapid, the heart's action weak and the tones faint this drug must be given in small doses or discontinued; myocardial weakness may already be near the danger point. When sodium salicylate is poorly tolerated toxic symptoms may appear, among which are a slow, feeble pulse, tinnitus, deafness, headache, delirium, vomiting, general weakness and dyspnoea. There may be polyuria. These should be regarded as warnings of a possible impending cardiac weakness or even collapse. According to Lees a full dose of sodium salicylate for an adult is 20 to 30 gr. (1.3 to 2 gm.) every two hours, sodium bicarbonate in the same or larger amount being given with it. Few physicians give such large doses. If given, there must be extreme caution and smaller doses are safer and usually suffice. Acetyl-salicylic acid may be substituted for the salicylate.

Digitalis is seldom indicated in these acute cases. Yet, if the process is a recurrence and the heart already the seat of an old valvular or myocardial lesion, if there are signs of heart failure, and particularly if auricular fibrillation sets in, digitalis is to be given. The need of giving it when there is an acute carditis seldom arises but the danger from its use in such a condition is not as great as is sometimes feared.

Cold, as an ice-bag to the precordium, sometimes relieves distress or pain. It at least has a suggestive value in making the patient feel that something is being done and it helps to keep him quiet. Any influence in allaying the inflammatory process is doubtful.

The diet should be simple and easily digestible, proteins being sparingly allowed. The bowels may need an occasional laxative or an enema. Restlessness may call for bromides, veronal or some opiate.

In convalescence great caution as to exercise is necessary. Not until the temperature has been normal for many days and the heart rate has reached a stationary point, as near to normal as it will go; not until the heart no longer diminishes in size; not until all unpleasant symptoms have disappeared, should the patient be allowed out of bed and about the house. Easy walking, preferably out of doors, the distance increased daily, may be the beginning of helpful graded exercise. All severe exercise should be interdicted for a long time. The heart can thus be tried out, its tolerance tested and its muscle strengthened. For the time being at least, it becomes competent for ordinary effort.

A most pressing need is for more and better accommodations for the poorer patients who are convalescing from acute cardiac disease. The ordinary hospital is rarely able to keep the patient as long as is necessary,

and home conditions too often are such that proper rest and supervision of exercise cannot be obtained, even with the aid of the social worker or visiting nurse. It frequently happens that the heart which, if afforded a few weeks or months more of relative rest, might have been brought back to a condition approaching normal, is left seriously crippled. Convalescent homes or hospitals specially equipped for the care of these patients are sorely needed. They would rescue many a cardiac patient from a state of incapacity for work and restore him to a condition in which he would be self-supporting.

MALIGNANT ENDOCARDITIS

There is a practical clinical distinction that generally can, and whenever possible should, be made between the simple and the malignant forms of endocarditis. Objection is often made to the use of the term malignant for the reason that some patients recover. It is also a harsh term to employ with the laity. This is all true. But similarly objection may be urged against the term ulcerative because many times there are no true ulcers on the valves. The terms infective or bacterial are employed but are objectionable as it almost implies that the simple form is not of infectious or bacterial character. We might better, perhaps, use the word "infecting," happily employed by Hanot, who speaks of this type as not alone infective but *infecting*. This brings out the fact of its microbic origin and its power still further to cause infection. We must agree with Horder, however, that the question of a name is of rather trivial importance. While no one name is entirely satisfactory and while the line between the simple and severe forms is not always easy to mark out, there is, nevertheless, a type differing from the simple in such a way as nearly always to permit of recognition and separate classification.

The feature to be kept in mind is that this disease is of the nature of septicemia. It is necessary to forget, for the time being, questions as to the competency of the valves, the muscular power of the heart, in short the mechanical function of the organ, if we are to have the correct conception of malignant endocarditis. Mechanical features may play a part, but the leading phenomenon is always the infectious or septic one which is usually so severe as justly to be termed malignant.

Frequency.—The disease is comparatively rare, though not so rare as believed by some. Even making allowance for overlooked cases, the general practitioner may go for years without seeing a case. The subacute form is more common than the acuter ones. In our larger cities, where puzzling and serious cases are rounded up in hospitals for study and consultation, these subacute cases are far from infrequent. Several times within a single quarter, I have been able to show to the students three or four of these patients in the Presbyterian Hospital under the care of my colleagues or myself. Horder's figures for St. Bartholomew's Hospital, 1901-1908, showed 115 cases of chronic infective endocarditis in 19,904 in-patients or 1 in 173, a remarkably high percentage, especially if by in-patients he refers to all kinds of patients, surgical, medical, etc.

Libman in hospital and consultation practice in New York has seen some 800 cases.

Etiology.—The most frequent organism is the streptococcus. In the subacute or chronic form the *Streptococcus viridans* is the prevailing germ. In the acuter types the hemolytic streptococcus is far oftener encountered. The pneumococcus, gonococcus, staphylococci, the influenza bacillus, the meningococcus and others may be responsible. The disease is not a unity etiologically and one might expect a different pathological anatomy and a different clinical course, depending on which germ was the infecting agent. To a certain extent this is true but the distinctions are rather slight and crude. It is not always possible to tell from the gross or even microscopic appearance of the lesion what organism is responsible and clinical differentiation is still rather imperfect. In many instances it is only by cultures of the blood during life or of the tissues after death that the question is settled. Some organisms, however, cause symptoms that are at least suggestive. Thus in the fulminating form due to the staphylococcus there is a fairly distinct picture. The clinical features of the subacute or chronic form caused by the *Streptococcus viridans* are quite clear-cut, as much so, perhaps, as are those of typhoid fever.

Acute malignant endocarditis is usually secondary to some other disease or springs from some recognizable primary source of infection, from which organisms enter the blood and lodge upon or invade the valves.¹ Thus it may be a complication of pneumonia, osteomyelitis, gonorrhœa, puerperal or surgical sepsis, etc. At times the primary focus is not discoverable but we must remember such foci as furuncles, a traumatized urethra, an infected gall-bladder, otitis, infected nasal sinuses, diseased tonsils and teeth. While the primary disease may have disappeared spontaneously or as the result of treatment, the lesion on the valve has assumed the leading rôle and continues the process generally until the death of the patient. In some cases, however, the valvular localization discovered only at autopsy may be viewed rather as an incident in a pyemic process which overwhelms the patient before the endocardial lesion has become of supreme importance or clinically recognizable.

Pathology.—The valves of the left heart are most commonly affected, the mitral a little more frequently than the aortic. At times both are involved. Right heart lesions are not uncommon as was noted by Thayer in the gonorrhœal form. The edges of congenital defects—patent ductus Botalli, perforate septum ventriculorum, stenosis of the aorta, etc.—are occasionally the site of the disease. As a rule grayish cauliflower-like vegetations project from the valves. These are rich in fibrin, platelets, red and white corpuscles and, as shown by culture or staining, contain the causal organisms, which may be on or in the fibrinous mass in huge numbers. The vegetation is commonly soft and friable, even exuding pus on pressure. In the subacute type these vegetations may be firmer,

¹ It is interesting to recall the first case of endocarditis of this form in which the direct relationship between the primary focus, a suppurating corn, and the cardiac lesion was recognized and in which microorganisms were demonstrated microscopically. The history and autopsy sound like those of a typical staphylococcus infection. The case was reported by Winge in Christiania in 1869.

manifesting proliferative changes, with quite solid bands running from the valves to the neighboring mural endocardium and to the chordæ tendineæ and no naked-eye pus may be seen. In more chronic cases the vegetations may be very hard, dry and scar-like, with no adherent thrombi. There may be lime deposits.

The difference between these large irregular, shaggy, fungus-like masses irregularly distributed over the valves, and perhaps the myocardium, and the row of firm small beads close to the edge of the valve in the simple form is very striking. No less striking is the fact that the process in the malignant type is more destructive. Loss of tissue can be plainly made out, often with the naked eye. The valve may appear worm-eaten or frayed at the edges; it may be so weakened as to bulge in an aneurismal manner or may be perforated. These are the so-called ulcerative changes. They are often seen on the mural endocardium with excavating ulcers with necrotic margins or extending out along the tendinous cords. The chordæ may be broken. Briefly the condition might be described as similar to a suppurative inflammatory process in any other part of the body with its attendant exudative, destructive changes, its invasion of the deeper structures and of surrounding tissue and with a varying tendency toward repair. The ease with which emboli may be swept into the circulation from such a lesion is evident and it makes readily understandable the toxic and embolic phenomena of the disease.

ACUTE MALIGNANT ENDOCARDITIS

Clinical Features.—Two classes of malignant endocarditis may well be made, the acute and the subacute or chronic. These cases shade one into the other, so that a given case might be regarded as acute by some, and chronic by others.

In the *acute* form there is commonly a primary recognizable cause; the disease is not cryptogenetic as is so often the case in the chronic type. This form accompanies or follows pneumonia, staphylococccic osteomyelitis, puerperal septicemia and gonorrhœal bacteremia. The onset is often abrupt with a chill and prompt rise of temperature. The constitutional effects are marked, prostration, often mental apathy or delirium and the group of symptoms referred to as "typhoid." In some of the hyperacute or fulminating cases, as are not infrequent in endocarditis due to the *Staphylococcus aureus*, the course is rapid and the manifestations virulent. Chills may be repeated at irregular intervals, the temperature rising with each chill, perhaps to 104° to 106°. Following the chill, fever and sweating, there may be an afebrile period of a few hours and then the paroxysm is repeated. At times the chills and fever are quite regularly periodic, at other times the fever is more remittent. The grouping of these cases made by Eichhorst is very helpful *pyemic* with high, irregular fever, chills and sweats; *malarial* with febrile paroxysms at regular intervals; and *typhoid* with a regular remittent type of fever. Of course, there is no malaria or typhoid fever in the sense of an infection with the specific germs of these diseases. It is merely the resemblance to the temperature curves of these diseases to which attention is called;

this serves to impress the fact that the fever is very variable. The blood usually shows an increase in the polynuclear leukocytes. The organism may generally be found in blood cultures.

The *spleen* is generally palpable and may be tender when the seat of infarcts. The urine may show a trace of albumin or even the findings of an acute nephritis.

So far there is nothing distinctive about the condition described. It is merely a septic or pyemic state often regarded as a manifestation of a blood infection secondary to the primary disease and such it really is. The involvement of the heart is revealed by two facts particularly, the evidence by murmur and other local signs that there is cardiac disturbance beyond what the fever alone would explain, and the appearance of embolic phenomena.

The heart may or may not have been the seat of an old valvular lesion. If not, the murmur is a new feature. It may be at any valve, commonly the mitral or aortic, and may be such as is found in regurgitation or obstruction. It is usually so frank in its loudness and quality as to lead one at once to regard it as definitely organic and not one of the so-called accidental murmurs. The heart may increase in size, is rapid and may manifest various irregularities. New features in the murmur may appear, as a change in timbre or the appearance of a diastolic murmur when only a systolic had been present before. These indicate that an acutely changing process is present in the heart. In other cases there is an old valvular disease that may long have been recognized. This may or may not show some change in physical signs as the acute process is added to the chronic, which latter condition has really favored the localization and development of germs. Often, however, the storm of symptoms of the primary disease, such as osteomyelitis with pyemia, a severe pneumonia or a tragic puerperal sepsis, may occupy attention and cover up the real significance of the altered heart tones or the new murmur.

The *embolic phenomena* are often of extreme help in diagnosis. Petechial spots in the skin, a few to many hundreds in number, are the most common. Usually these are small, pin-head sized, although at times there are larger ecchymotic lesions, some of which are confluent and others evidently due to an hemorrhagic tendency. The elder Janeway described small reddish nodules that appear especially in the palm of the hand or the sole of the foot. These are painless, last for a few days and disappear. Larger emboli may plug arteries of considerable size, causing gangrene of an extremity, hemiplegia, an infarct in the spleen or kidney, etc. These are considered more at length in discussing the chronic type. Only rarely is there suppuration about these embolic deposits, usually merely an acute reactive inflammation. In some instances, however, especially with the staphylococcus, suppuration occurs.

Probably some of these patients recover but the number is certainly small. In the most virulent types death may occur in three or four days, the whole process being comparable in its malignancy to the fulminant forms of scarlet fever or smallpox. More often the patient lives for two to four weeks, perhaps even two months, gradually losing ground, becoming weaker, thinner and paler, with complications such as acute nephritis,

pericarditis or pleurisy; with the heart more rapid, the blood-pressure lowered, murmurs persisting, perhaps cardiac irregularities, or with dyspnoea, cough and oedema. The tongue becomes dry, the breath foul, the mind may be dulled and there may be incontinence of the bladder and bowels; in short he may exhibit all the manifestations of the "typhoid state."

SUBACUTE AND CHRONIC MALIGNANT ENDOCARDITIS

There is a fairly well-defined form of malignant endocarditis that runs its course in from two months to one year, occasionally being prolonged for two years. This is frequently classed as chronic. The larger number of these cases last from two to six months and might better, perhaps, be grouped as subacute. Cases of this type are much commoner than the acuter form just described.

While various organisms may cause this form—the pneumococcus, gonococcus, staphylococcus, influenza bacillus, etc. the prevailing type, in 95 per cent. according to Libman, is the relatively non-virulent form of streptococcus, the *Streptococcus viridans* of Schottmüller, found so often in the mouth, about the teeth and in the tonsils. In what percentage of cases the organisms come from these sources one cannot say. It is suggestive, that not infrequently a few days or weeks before symptoms of the endocardial condition become manifest there has been a tonsillitis, a periapical abscess or a nasal infection. Next in frequency as a cause, but second by a long interval, is the bacillus of influenza. The hemolytic streptococcus rarely if ever causes this chronic form of endocarditis.

One fact is agreed upon by all observers, that a large majority of patients with this disease are already sufferers from valvular lesions, the result of preceding infections especially rheumatic fever or chorea. Only rarely has the preceding damage been due to syphilitic or atherosclerotic change. Occasionally the acute process arises at the site of a congenital defect. The valve as though traumatized has become a *locus minoris resistentiæ* and the lodgment and activity of germs are favored. While many of these patients in earlier years have had acute rheumatic endocarditis it is rare to see the direct passage from a first attack of acute rheumatic (simple) endocarditis to the malignant form.

Germs roused to activity, in the throat for example, presumably enter the blood-stream in goodly numbers, lodge in the vessels of the valves, induce hemorrhages and reactive inflammation, leading ultimately to roughening, necrosis and giving way of the serous covering of the valves, on which appear deposits of fibrin with rich content of red and white corpuscles and bacteria. Or as many believe, the lodgment of the bacteria is directly from the blood-stream more upon the valve than in it. The lesions tend to progress. Valve structure is destroyed, the mural endocardium may be involved by contact or implantation, the fibrinous mass may project as a friable, cauliflower-like excrescence from which bacteria-containing fragments may from time to time be detached or which may almost continuously permit of the escape of bacteria and toxins. The essential feature is this lesion of the valves which acts as a

reservoir and factory of germs and which for some reason shows little tendency toward spontaneous recovery or complete healing.

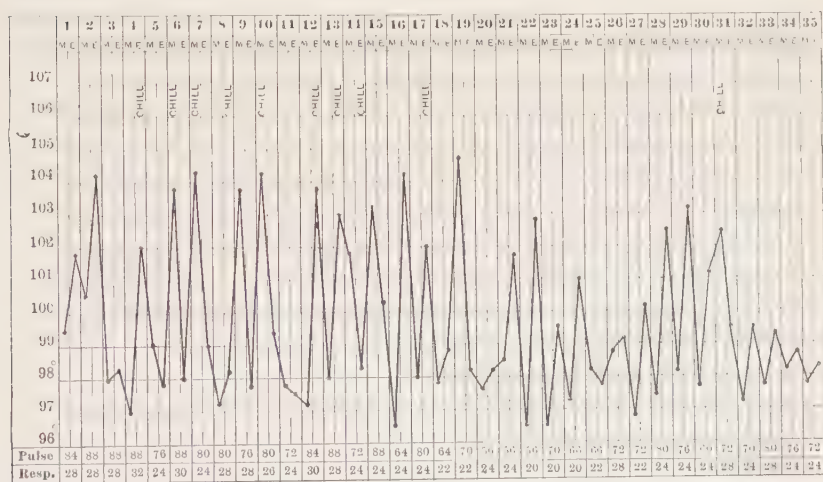
To this statement some exceptions must be made. Occasional recoveries from cases diagnosed as ulcerative endocarditis by competent men have been seen. In valves, the seat of an active process, fibrous areas that represent healed patches are sometimes seen. So we may say that healing is possible but in cases clinically recognized as this type of endocarditis it is extremely exceptional. Some of the instances of healing found postmortem are in patients who have probably suffered from a milder type of chronic endocarditis unrecognized during life.

Symptoms and General Course.—We may picture a typical case as occurring in a young adult with a mitral or aortic lesion from rheumatic fever in childhood but whose heart is functionally good. Malaise, fatigue, poor appetite, vague aches in different parts of the body and perhaps joint pains appear insidiously. The patient's color is not as ruddy as before and some day it is discovered that he has fever, perhaps a temperature of 100° in the evening. He gives up work for a time and rests but the symptoms persist and the fever occasionally reaches 101°; there is some loss of weight; the sleep is poor; the patient grows weaker and paler; there may be some pain in the joints, over the spleen or at the tips of the fingers. Examination shows a secondary anemia, an enlarged spleen, a pulse somewhat increased in rate and the heart with its previous enlargement and familiar murmur. Perhaps a few râles are heard in the chest and tuberculosis or typhoid fever may be suggested. It may be that the endocarditic nature of the attack is disclosed only when a crop of petechial spots is noted or when the *Streptococcus viridans* is found in a blood culture. Week after week the course of the disease is monotonously the same although there is a gradual loss in strength and weight. Then perhaps some frank embolic manifestation appears, an infarct in the spleen or kidney or the plugging of a large vessel as of the brain or arm, or a huge crop of petechial spots is seen. The fever becomes higher and more irregular; there may be chills; an acute nephritis may develop; the heart action becomes poorer and after several months the patient succumbs to exhaustion, a secondary nephritis, cardiac failure or to some embolic accident.

Onset.—Occasionally this is abrupt; occasionally the first symptoms are clearly cardiac. As a rule the onset is insidious and often remarkably like that of typhoid fever. Rarely is a patient able to state the exact date of the onset. The first symptom may be headache or fleeting pains in other parts of the body. He may feel that he has overworked because he is easily tired and lacks his usual energy and endurance. He loses his appetite. His color is not what it was and he may have lost a few pounds in weight. He is, according to his own diagnosis, a little "run down" and needs a tonic or a rest. It is to be noted that there are no symptoms that directly call attention to the heart; it is as competent to do its mechanical work as before. The patient and the physician may not suspect the cardiac origin of these symptoms, fearing rather typhoid fever or tuberculosis when the fever is discovered, or thinking the whole trouble is due to overwork, neurasthenia, etc.

Temperature.—Sometimes chilly sensations with a feverish feeling following make the patient aware at an early stage that he has fever. At other times it is only the routine examination that leads to the discovery that the temperature is elevated. Nearly always there is a daily rise of temperature, generally toward evening. The morning temperature may be normal, subnormal or somewhat elevated. We have, therefore, over a period of from two months to a year or more an intermittent-remittent type of fever, with ups and downs, often for several weeks or months no record being above 102° and perhaps periods of a day or several days when the temperature does not pass 99° . These possible afebrile periods should not be forgotten as otherwise they may throw us off our guard as to the serious nature of the illness. Exacerbations of the fever may occur due to complications such as an acute pericarditis, pleurisy or large splenic infarcts. At other times no local lesion explains the sudden rise, though chills and new petechiæ may lead us to suspect that an unusually rich supply of toxic material has been showered into the circulation. Elevations to 104° or 105° are then not unusual.

FIG. 29



The temperature curve in a severe case of endocarditis.

The main fact to be remembered about the fever is that it follows no rule; it may be intermittent, remittent or pyemic in character, or all three if long observations are made. It may even show afebrile periods of many hours or several days, but it is remorselessly persistent continuing week after week or month after month until the end. Once in a gonorrhœal endocarditis I saw an afebrile period of a week just before death. Similar observations of terminal apyrexia have been made by others.

Toxic and Constitutional Symptoms.—These have already been mentioned in discussing the onset. They vary much in intensity and in their rapidity of development. Some patients keep at work long after they

know they have fever, insisting that they are only slightly tired or a little indisposed. In this respect they resemble some patients with tuberculosis. But as the illness progresses the weakness is such that the patient is more and more indisposed to be about and keeps to his room or his bed voluntarily. He may complain of arthralgic pains or of vague pains in different parts of the body or may have no pain.

The *appetite* is apt to be less keen and digestive disturbances such as a coated tongue, a bad taste in the mouth, belching of gas and irregular bowels may be annoying. Sleep is poor; the patient may be apathetic or at times apprehensive, nervous and irritable. There is loss of weight. As the disease progresses and especially if complications set in such as nephritis or pyemic manifestations, the toxic symptoms become more marked; there is greater prostration, often sweating, a dry tongue, pronounced apathy, trembling of the hands and later, delirium and even involuntary discharges.

Heart and Bloodvessels.—The heart shows the signs of a valvular lesion generally of the left side, a mitral leak or obstruction or an aortic regurgitation, rarely an aortic obstruction. Right-sided lesions must be watched for; they are by no means to be ruled out on the basis of rarity. The right-sided lesion is usually associated with a left-sided lesion. When, as occurs rarely, it is isolated, unassociated with mitral or aortic defect, the signs and symptoms may be very misleading or masked. Emboli, for instance, pass into the pulmonary circuit rather than into the systemic circulation.

The ease with which the acute endocardial lesion is overlooked is readily understood when we remember that in so many instances there is an old valvular defect long known to patient and physician. On examination the heart is found of the same increased size as for years before; the murmurs show no appreciable change in quality; there is no irregularity and only a moderate increase in rate; there is no complaint of dyspnoea, cough or precordial distress; there is no cyanosis or oedema; in a word there is no symptom or sign of cardiac failure and the heart seems as before. Familiarity with its defects has bred contempt for them. No wonder that so often the heart is passed as innocent of offense in these cases, and the physician only gets back to it as the guilty organ after he has carefully excluded all other sources of disease or has had his attention sharply drawn to it by some obtrusive embolic phenomenon. Or—to use the vernacular—the blood culture may “put him wise.”

The acute changes in the valves may so alter physical conditions as to lead to changes in the character of the murmurs. New valves or the chordæ may be attacked, the vegetations may change in size and shape owing to new fibrinous deposits or loss of substance as portions liquefy or slough off and are carried to distant parts of the body. The change in physical signs is, however, not as common as it is sometimes thought to be. The murmurs are apt to remain unchanged in character. Yet occasionally one recognizes that an aortic leak has occurred overnight or within a few days and suspects a perforation of a valve; or the quality of a mitral murmur changes so markedly as to leave little doubt that some acute process has brought about the alteration.

As the disease progresses the heart's action becomes more rapid. At first the rapidity may be evident only on exertion but later the rate may be 100 or more with the patient in bed. Irregularities, such as extrasystoles, may appear. The heart may show dilatation by an increase in its area of dullness and a shift of its point of maximum impulse to the left. The blood-pressure is commonly low.

In many patients there is from beginning to end no real cardiac failure. Mechanically the heart stands up to its task. In others the weakness of the myocardium begins to show in an irritating cough, dyspnoea on movement, more rapid and more irritable pulse, some cyanosis, engorgement of the liver or œdema of the ankles. In some instances, particularly those in which there is secondary nephritis, œdema may be extreme. Clubbing of the fingers may be noted even when there is little evidence of cardiac weakness. Sudden cardiac failure may terminate life.

Blood.—(a) *Anemia*.—Anemia is the rule. This is of the secondary type with a relatively greater reduction in hemoglobin than in the number of red corpuscles. The color index is below one. At times the pallor is so pronounced as to suggest a severe hemorrhage or a pernicious anemia. Twice I have seen an unusually low blood count, the hemoglobin being in the twenties and once the red cells were around 1,000,000. There is rarely any improvement in the blood condition. In spite of rest, diet, fresh air and drugs the degree of anemia gradually increases.

(b) *Leukocytes*.—The leukocytes vary in number. While in the acuter and more virulent types of malignant endocarditis there is generally a polynuclear leukocytosis, this is not marked in the chronic type due to the *Streptococcus viridans*. Blood counts of 7000 to 15,000 are common with the slight increase due to the larger percentage of polynuclear cells. Higher figures are met with. In a recent case lasting several months there were many counts showing over 30,000. Some patients show no quantitative or qualitative change. This absence of leukocytosis should not lead to the exclusion of malignant endocarditis, an error not infrequently made.

(c) *Bacteria*.—Bacteria are nearly always to be found in the circulating blood if careful technique is employed and if, when a negative result is obtained, the search is not given over but is repeated. Enough blood must be taken, care must be exercised to keep tubes, flasks and plates at a proper incubation temperature and time must be allowed for the development of organisms which may grow slowly and which may be present in small numbers only. While there is no one most favorable time for finding the organisms in the blood it has seemed as though they were more likely to be found if blood cultures were made at the time of a chill. In some cases, however, several blood cultures may be negative though at autopsy active bacteria may be present in large numbers. In others instances the negative blood cultures are due to the fact that the patient is seen in the bacteria-free stage or stage of spontaneous recovery, to which Libman has directed attention and to which reference will be made later.

(d) *Hemorrhages*.—Hemorrhages into and under the skin—petechiæ—are commonly regarded as due to minute emboli. But at times there seems to be a tendency to hemorrhage much as in purpura. Large

ecchymotic spots are seen; there may be nosebleed; the gums ooze blood; the retina is crowded with hemorrhages; the mucous membranes may bleed. This tendency is to be remembered as it may lead to confusion in diagnosis.

Spleen.—Enlargement of the spleen is practically always present and can usually be made out on careful palpation. Rarely the spleen may be prevented from descending with deep inspiration by adhesions due to preceding inflammation. Horder refers to a case in which the spleen, though large, was not palpable because of a well-developed costosplenic ligament on which the spleen rested.

The splenic enlargement may be due to any one of four causes, very often to a combination of two or more of these causes: (a) Acute splenic tumor as in other infections. (b) Passive congestion when the heart's action is weak, a cause not very potent but of some influence. (c) Emboli lodging in the viscus producing infarction with (d) inflammation including perisplenitis. Often the spleen at autopsy is seen to contain several old or recent infarcts with some areas swollen while some of the older ones show scarring and retraction.

From the clinical point of view the careful consideration of the spleen is of extreme importance. The point to be remembered is that it is often the seat of infarcts, with inflammatory reactions, that involve the peritoneal covering and induce both an increase in the size of the organ and pain. A very suggestive fact in the history of many patients with ulcerative endocarditis is that there has been pain, perhaps severe pain, in the left side toward the costal margin. There may have been several attacks of such pain. Close questioning may bring out the fact that the pain came on suddenly. Often the patient will locate it at or just below the left costal margin. It is frequently, particularly in cases in which the diagnosis of malignant endocarditis has not been made, regarded as due to acute indigestion, stomach trouble or to pleurisy. Color is lent to the latter diagnosis by the fact that the pain may be referred to the chest, aggravated by deep breathing or coughing and because a friction with respiration may often be heard due to perisplenitis. Only searching inquiry as to the exact mode of onset of the pain and careful examination of the splenic region will enable one to recognize the real condition. The friction due to perisplenitis is low down and may at times be elicited *below* the costal margin by pressure of the stethoscope or be heard there on deep breathing. The spleen is palpable and on moving it pain is caused. At times the site of the infarct and its size have been mapped out by palpation. At least this is reported by observers, though one will rarely have the courage to interpret the findings so definitely.

Skin.—(a) Sooner or later in nearly every case small pinhead-sized purpuric spots appear in the skin. These are at first rather bright red or purplish; the color does not disappear on pressure. In a few days the small extravasation of blood is absorbed and the color fades. These spots may appear on any part of the body. They are often grouped about a shoulder, at the bend of the elbow, over the lower abdomen or on the dorsum of the foot. These groups, suggestive of a shower of minute emboli, may consist of half a dozen spots or the number may be in the

hundreds. At other times the spots in small or enormous numbers are scattered indiscriminately over the body. They may be found also in the conjunctiva, the retina, or the mucous membrane of the mouth. So important are they as diagnostic aids that most careful search should always be made for them. Even a few, if unquestionably of petechial character, may give the diagnosis. A permanent small, bright reddish, slightly elevated telangiectatic maculopapule often found on the skin of the chest must not be regarded as one of these lesions. Confluence of small spots may lead to purpuric lesions 2 to 3 mm. in diameter.

These petechiæ are generally regarded as due to mycotic emboli, as really infarcts in the skin. They are often described as having a pale, anemic centre. This is probably true though one must not expect to see this always. Usually the color is uniformly distributed throughout the lesion. The occasional hemorrhagic tendency leading to fair-sized ecchymotic areas has been noted. Their occurrence lends some weight to the belief that these petechiæ are not in every instance embolic in origin.

It is very rare indeed for one of these lesions to be followed by suppuration. In staphylococcus infections metastatic suppuration, as has been said, is apt to occur, but with the *Streptococcus viridans* multiple embolic abscesses in the skin or elsewhere in the body are practically unknown.

(b) It happens quite frequently, and it may be an early phenomenon, that emboli lodge in capillaries or arterioles in the toe, tips of the finger, palm of the hand, or sole of the foot. There is a rather sudden pain and a little reddened swelling which is tender to pressure. These small nodules last for one or two days and gradually disappear. Local redness may mark their site for a day or two even after the acuter pain has gone. I have seen larger areas of the same nature at the bend of the elbow when the resulting redness was 2 cm. in diameter. The patient may think little or nothing of these tender lesions, he regards them as trivial or as a manifestation of "rheumatism." They should, therefore, if not mentioned by the patient be inquired after and searched for. One must agree with Osler in the emphasis he placed on their diagnostic value.

(c) Occasionally rashes of an erythematous or maculopapular nature, resembling those of scarlatina or measles, are seen. They are not especially characteristic of malignant endocarditis. These are on the order of the toxic rashes seen in other types of septicemia.

(d) *Jaundice* has been reported but is not common in the chronic form under consideration. In the more virulent types or in the acute exacerbations of this chronic form an icteric tint of the sclera is occasionally noted. This as in other septicemic conditions may be polycholic; the possibility of complications as cholecystitis, cholangitis or abscess of the liver should be kept in mind.

(e) In some cases the skin is darker than normal, the *café au lait* pigmentation of Libman. The same author also refers to a brownish pigmentation seen in patients who are in what he terms the bacteria-free stage of the disease.

Kidney. A trace of albumin with a few hyaline casts is very common and of no special value for diagnosis nor does it speak for any real complication. It is the febrile albuminuria common to many infections.

But there are two renal conditions in this disease that may be helpful in diagnosis and materially affect the symptomatology and the course—*infarct* of the kidney and *acute nephritis*. Many small infarcts—this is shown by autopsy—occur in the kidney without producing symptoms that attract the attention of either patient or physician. Loehlein, Baehr, and Libman call attention to the frequency with which in this form of endocarditis due to the non-hemolytic streptococcus lesions due to minute emboli may be found in the glomeruli of the kidney. Not all glomeruli are involved nor even all of a single glomerulus. This is not a nephritis though it may pave the way for later development of that condition. Red blood corpuscles in the urine on microscopic examination are found not infrequently and may point to such embolic obstruction of a small renal vessel. But with larger emboli and a greater area of infarction there may be hematuria of considerable degree, enough blood being passed to color the urine red and to attract the patient's attention. He may suffer from severe pain in the back, at times with many of the characteristics of renal colic.

It need not excite surprise that the kidneys, eliminating toxins and the seat of emboli, ultimately become acutely inflamed. This inflammation is generally rather frank in its manifestations, showing its presence by œdema of the eyelids, face, ankles, etc., and by an abundance of albumin in the urine with numerous casts of various kinds, and a liberal number of red blood cells. The amount of urine may diminish. Occasionally there is some complaint by the patient of frequency of urination, a slight burning in the urethra or of an ache in the back, but these subjective symptoms are often lacking. This nephritis is often of serious import and hastens the progress of the disease. Headache, drowsiness, loathing for food and disturbed digestive functions are partially explained on the basis of renal insufficiency. The blood chemistry may confirm the existence of this condition. A physician seeing such a patient for the first time when this acute nephritis is manifest, did he not know the past history, might easily regard the œdematous toxic patient as having nephritis only. The secondary nature of the renal disease might escape his attention.

While a nephritis of an outspoken character with marked œdema has been described it must be noted that in some cases—in my experience rather exceptional—the nephritis does not produce noticeable œdema; it is discovered only by the routine urinalysis.

Emboli.—A French writer has well said that we owe our understanding of malignant endocarditis to the work of two men, Pasteur and Virchow. Pasteur revealed to us bacteria and sepsis; Virchow explained embolism. Nothing is more characteristic of malignant endocarditis than its embolic manifestations. Some of these have little influence on the state of the patient or the course of the disease and may be viewed as symptoms; others are of more serious character and assume the proportions of complications. Some of these embolic phenomena have already been discussed—the petechiæ, the painful spots of Osler, and infarction of the spleen and kidney. The two first may be classed as of symptomatic or diagnostic importance only, the two last may be at times more serious.

Embolic obstruction of a *cerebral artery* occurs not very infrequently.

If some large artery is plugged sudden death may occur, or hemiplegia with or without unconsciousness. The manifestations are the same as in cerebral embolism from other causes. Recovery or improvement is not at all impossible; in fact, some improvement is frequently noted. Only rarely is suppuration produced about a non-hemolytic streptococcus embolus of the brain, though a streptococcus form of meningitis has been described in these cases. Smaller emboli or the plugging of a smaller artery may lead to a great variety of cerebral disturbances. A monoplegia may occur and several times I have seen aphasia. These paralyses may be only partial; they are often temporary. A transitory forgetfulness, mental clouding, garrulousness, dizziness or diplopia may have their origin in the obstruction of a small branch by minute fibrinous masses which lodging in the skin might have produced petechiæ or painful spots. Horder refers to choreiform movements in 7 cases—in 4 early in the disease—and regards these as probably cerebrally embolic in origin. In Horder's 150 cases there were 22 instances of cerebral embolism.

Emboli in the *retina* may be symptomless. Often numerous hemorrhages may be seen with the ophthalmoscope though the patient has no difficulty of vision. In the older works these retinal hemorrhages were regarded as proof of the malignant or ulcerative nature of the endocarditis. One cannot place quite so much value on this finding as did the earlier writers but their frequent occurrence is to be remembered. Emboli obstructing the central artery of the retina or involving the macula or inducing large hemorrhages naturally cause visual disturbances. Lesions of the iris seem to be rare.

The *peripheral vessels* may be obstructed and gangrene result. I have seen in one case gangrene of a foot and in another of the leg due to obstruction of the popliteal artery; in another extensive gangrene resulted from obstruction of the external iliac artery, in another gangrene of one leg and one arm. At times one may recognize an embolic plug in an artery by the pain, local tenderness, loss of pulsation, altered color of the part, etc., and yet the expected gangrene does not occur, collateral circulation being sufficient to prevent it.

Among the peripheral vessels may be included the *mesenteric* arteries. Complaints of abdominal pain should not be passed over lightly, as this may be evidence of mesenteric obstruction. Tympany, tenderness, nausea, perhaps bloody stools, with more or less of collapse may give the diagnosis. Virchow and Oppolzer reported atrophy of the liver through obstruction of the hepatic artery.

Pulmonary embolism may be a serious incident in malignant endocarditis. This may occur when the valves of the right heart are involved. Because of the usual left heart lesions those of the right heart are frequently overlooked, attention being focussed on those of the mitral and the aortic valves and the murmur over the pulmonary area being regarded as a part of the mitral murmur or as an accidental murmur. Under these circumstances a pulmonary infarction may come as a great surprise and lead to confused notions as to its nature, pneumonia or pleurisy being considered because of the pain, dyspnoea, cough, blood-tinged sputum, friction rub, râles, etc. The possibility of right heart malignant endocarditis should not be forgotten.

A very puzzling and instructive case came under my observation a few years ago, in which many physicians tried their diagnostic skill and all failed. The autopsy showed there was an acute endocarditis of the pulmonary valves alone. The faint systolic murmur heard during life had been regarded by all as an accidental murmur. The malaise, moderate anemia, slight irregular fever, loss in weight and an occasional trace of albumin had led some to diagnose, at least tentatively, a pulmonary tuberculosis, a diagnosis rendered more probable because of an occasional cough, with a few fine crackling râles in one spot in the chest, and because at this time—the occurrence was repeated once or twice—there was expectoration of a little blood. Blood cultures and sputum examination had shown no organisms of any special disease. It was only when the autopsy revealed the ulcerative lesion of the pulmonary valve with infarction in the lung that the previous history became intelligible.

Emboli may lodge in the *vasa vasorum* or in the coronaries. In the latter case sudden death might take place or an anginal attack occur followed by myocardial softening with evidence of weakness of the heart. When an embolus lodges in the wall of a vessel it may lead to such a weakening of the wall as to cause a bulging—a true aneurism. These mycotic aneurisms may affect any vessel and may be multiple. I saw one in a branch of the gluteal artery with a resulting aneurism half the size of a man's fist. Later a second aneurism appeared on the facial artery. Horder found 20 instances of mycotic aneurism in 150 cases.

It may seem like wearisome repetition to call attention once more to the importance of keeping one's eyes open for these embolic phenomena. But this feature may properly be emphasized because it is so important and so often overlooked or misinterpreted. The tender spots are ignored, the petechiae not seen, the complaint of dim vision or difficulty in getting the right word passed by as a vagary of an invalid, and the pain in the splenic region called neuralgic or pleuritic. In some instances there seems to be what might be called an embolic tendency, one manifestation succeeding another making a most bizarre and dramatic picture, as in a woman seen with Dr. Bassoe. She had come under his care for facial paresis, which he recognized as having its origin in an acute left heart valvular lesion. We saw in this patient during a few days not only the cerebral embolism, but gangrene of the foot from obstruction of the popliteal artery, pronounced hematuria with renal colic from renal infarction, and mesenteric obstruction as shown by abdominal pain, meteorism, collapse and bloody stools. The autopsy showed all these and numerous other embolic manifestations.

Diagnosis.—This disease, like so many others of comparative rarity, is oftener overlooked because not thought of and therefore not sought for than because of ignorance on the part of the practitioner. Once suspected, the search usually discloses some tell-tale symptom or sign and the diagnosis is reached. There are several misleading features that cause difficulty, misleading largely because they are not in accord with what is the picture of the disease in the mind of the physician.

Paradoxical as it may seem the greatest stumbling block to a correct diagnosis of malignant endocarditis has been the fact that there is and

has been valvular disease of the heart. Its long existence known to patient and physician and its failure to cause the ordinary symptoms of cardiac disease lead to its being ignored. The doctor views it with no more concern than he does the fixed hip joint the result of a tuberculosis in childhood. The lesions are pictured in his mind as healed, as things of the past. But the possibility of a flare-up of an old endocardial lesion should be thought of just as the thought might come in the other case that there might be a lighting up of a long dormant tuberculosis. It is a safe frame of mind to be in when studying a case of fever in a patient with an old rheumatic endocarditis to *think* at once of the possibility of acute endocarditis but not to *make* such a diagnosis until other diseases have been excluded.

Another source of uncertainty is that many times no primary cause, no portal of entry for the germs, can be found. It is to be remembered that while we assume that there is such a port of entry it may escape our notice. We are not justified in excluding a disease because we cannot find the exact mode of its origin. Painstaking search is often rewarded by the discovery of what may be presumed to be the origin; it is nearly always difficult or impossible to *prove* the origin. Not infrequently, a preceding tonsillitis, rhinitis or sinusitis, or an acute infection about a tooth has occurred. This may have quieted down; after the invasion of the blood by the germs, there often seems to be a period of incubation of one to four weeks. Such foci must therefore not be overlooked.

Many times I have had the diagnosis of malignant endocarditis questioned or even denied because there was no evidence of cardiac insufficiency. The fact that this disease is not one in which cardiac weakness is the central feature but one whose essence is infection and sepsis cannot be too forcibly emphasized. Absence of dyspnoea, cyanosis or œdema is no argument against the presence and activity of pyogenic organisms on the valves of a heart that may be doing efficient work from the mechanical point of view.

Again, the absence of leukocytosis has been misleading. The only answer to this objection to a diagnosis is the flat statement that in many cases of malignant endocarditis there is no increase in the number of white blood corpuscles, this being particularly true as regards the sub-acute or chronic forms.

The peculiarities of the fever are not always known. The long drawn-out character of the fever, extending perhaps over many months must be remembered. Several times I have had the diagnosis questioned because of the fact that "it would be impossible for an acute endocarditis to cause such a prolonged fever; the patient would not live that long; it must be hidden tuberculosis or pus somewhere in the body." The only answer to this is to draw attention to the fact that it is a pus infection—an infection of the heart valves and through them of the entire body and that prolonged fever is not unusual.

A colleague informs me that he once saw at autopsy an acute ulcerative endocarditis of the aortic valves in which case no murmurs had been heard during life. No such case has come under my observation but one may easily understand how an absence of an endocardial murmur would be

misleading. Romberg calls attention to the paucity of cardiac signs, especially clear-cut organic murmurs, in some cases.

Finally one may easily be unduly influenced by the prominence of some especial feature of the disease which, in reality a complication, stands out so strikingly as to lead one to look upon it as the main or primary disease. We may see the patient when there is a well-developed acute nephritis with marked œdema, albuminuria, hematuria, etc. The picture may be that of severe purpura rheumatica or hemorrhagica. I have twice seen the anemia so severe as to lead one to suspect the pernicious type or some severe hemorrhage. The case with multiple emboli already cited had been sent to Dr. Bassoe because of its neurological character; such nervous features may be misleading unless the cause is sought. Dr. B. W. Sippy once showed me a young man with an acute gonorrhœal malignant endocarditis—blood cultures were positive—who had been brought to him because of an acute diabetes, presumably an involvement of the pancreas in the acute infectious process. Romberg had 2 cases with autopsy in which the enlarged spleen with anemia led him to diagnose pseudoleukemia. Libman calls attention to the resemblance to splenic anemia, especially when there is little or no fever.

Differential Diagnosis.—When *typhoid fever* was a common disease in Chicago I saw several cases of malignant endocarditis that were regarded as typhoid fever. At this time blood cultures were not often made and the Widal test was not in general use. The resemblance is often rather striking. There may be the same insidious onset with malaise and chilliness; headache; the temperature chart may show similar remissions; there may be mental apathy; the spleen becomes palpable; the blood count may show no leukocytosis; the rash may, unless studied critically, be regarded as significant of typhoid fever.

But there are differences that sooner or later enable one to rule out the latter disease. In the endocarditis not only is there the valvular lesion but the pulse is usually more rapid. The spleen in typhoid fever is rarely tender and pain as from an infarct is not present. The blood in typhoid fever commonly shows a leukopenia; in endocarditis there is a normal or slightly elevated white count but not a leukopenia. The spots are clearly hemorrhagic in endocarditis; the color does not disappear on pressure; they are often located in groups and not by any means situated by preference on the abdomen. Blood cultures show in many cases of typhoid fever the bacillus of that disease and in endocarditis some other organism. The Widal test is of great value. A known source of infection for either disease might carry some weight. Typhoid fever in a patient with an old valvular lesion may be perplexing.

Malaria ought to be easily excluded, in spite of the regularity of the febrile rise, the large spleen and the absence of leukocytosis, by the study of the blood. The old rule that a malarial fever which does not yield to quinine should lead to a change in diagnosis holds here.

The resemblance to *pulmonary tuberculosis* may seem far fetched but it may be quite striking. The insidious onset, low-grade fever, secondary anemia, loss of weight and strength, rapid pulse, and absence of known cause for these symptoms—the heart lesion is an old affair and disre-

garded—may make one suspect tuberculosis. If a slight cough develops and if a few localized moist râles are heard, especially toward the apex, or if a perisplenitis be interpreted as a pleurisy one may be excused for thinking hard over the question of tuberculosis. I have cited to my classes a case in which the physician refused to be convinced that the disease in his wife was not pulmonary tuberculosis until numerous petechial spots and emboli, one shutting off vision in one eye, made clear the endocarditic nature of the case.

Miliary tuberculosis may be simulated at times and must be carefully excluded before a given case is declared to be malignant endocarditis.

I do not remember to have seen malignant endocarditis mistaken for acute leukemia but I have seen the latter looked upon as malignant endocarditis. The fever, rapidly developing anemia, the hemorrhagic lesions in the skin the enlarged spleen and a loud endocardial murmur may make the resemblance quite strong. The blood examination ought to clear up the diagnosis quite promptly. In acute leukemia there is nearly always a relic of the original angina, hemorrhagic gums and enlarged lymph glands so that the nature of the illness becomes clear.

Whether in a case of *septicemia*, *e. g.*, a puerperal sepsis, there is involvement of the heart valves in this progressive type of endocarditis is a problem that occasionally demands time for its solution. Embolic phenomena are here of great help and the same is true of some cases of *rheumatic fever* with acute endocarditis. Involvement of the valves with persistence of fever, especially in the absence of signs of active arthritis, should lead one to be cautious in considering the trouble as simple or non-malignant. Time will clear the diagnosis by showing, if it is of the malignant character, the enlarged spleen and emboli; positive blood cultures are confirmative. Pericarditis and pleurisy are commoner in the rheumatic form.

Prognosis.—One is tempted to dismiss the discussion of the outcome of acute malignant endocarditis in a very few words. So rare are recoveries that one might almost say the prognosis is uniformly bad. Yet occasional recoveries might be assumed to occur as they are not so very unusual in other forms of septicemia even though virulent pyogenic organisms are responsible. Gonorrhœal endocarditis, commonly malignant in type and fatal in result, has ended in recovery. I have seen such a case, a chronic valvular defect resulting after recovery.

In some patients dead of malignant endocarditis the pathologist finds clear evidence of partial healing, along with the active process. There are also hearts with complete fibrous healing in which, from the marked destruction of valve structure perhaps with perforation or from the extensive scarring of the mural endocardium, there is warrant for declaring that the old process must have been of the ulcerative type. Furthermore, clinically diagnosed chronic malignant endocarditis in rare instances is followed by recovery. Several years ago I recorded a case of recovery in a boy, aged three years, although there was no bacteriological examination of the blood and it may have been an influenzal case. Since then in all the cases of acute malignant endocarditis I have seen death has been the result. Every patient with the subacute or chronic form in whom the

diagnosis has been established on the basis of an old valvular lesion, splenic enlargement, fever, anemia, petechiae or other embolic phenomena and positive blood cultures has died with one exception. In this case, shown me by Dr. Billings, a girl, aged twelve years, one year after leaving the hospital was reported free from fever. Dr. Libman of New York has had an unusual opportunity to study these cases and has seen 6 cases of recovery. Horder refers to occasional recoveries as do many other writers. But the percentage of non-fatal cases is extremely small. One may feel more hopeful of possible recovery in the case of children. Here I have met several cases that seemed on the borderline resembling recurrences of the rheumatic type or the beginning of the malignant. Some characteristic features of the latter were lacking and recovery followed.

In the acute virulent type death occurs in from three days to a few weeks. From these hypermalignant forms the course shades off gradually through the acute, subacute, subchronic and chronic types, in some of which death occurs after a year or even two years of illness. Horder had one case in which the patient lived two years and a remarkable thing was that the organism was a staphylococcus which usually causes the acuter forms of the malady.

Our notions concerning the possibility of recovery from endocarditis due to the *Streptococcus viridans* may have to be revised. It is probable that not a few cases are entirely overlooked either because through paucity of symptoms the patient fails to consult a doctor or because the mildness of the symptoms fails to attract attention to the heart. The character of the cases described by Oille, Graham and Detweiler of Toronto, Salus of Prague and others is illuminating. Apparently not seriously ill, there were symptoms attracting attention to the heart—fatigue, weakness, shortness of breath, palpitation, precordial pain, moderate anemia, fleeting pains in the joint or muscles, gastro-intestinal disturbances, restlessness, irritability, mild fever and positive blood cultures. There was ultimate recovery with evidence of valvular defect when the patients were reexamined after several years.¹ These may well be term *endocarditis lenta*, the *schleichende endocarditis* of Schottmüller. We cannot disregard these cases because they are not of the severe type fixed in our minds as the classic form, nor can we ignore them as perhaps cases of bacteremia due to the *Streptococcus viridans* but without endocardial lesions such as those described by W. W. Herrick and others. We may have to recognize a type of infection by this germ with endocardial localization in which recovery is not infrequent. The cases of Capps may also be cited, adults with lighter yet classic features of the disease, who after many weeks recovered symptomatically, becoming fever-free and with no bacteria in the blood.

Strong proof of recovery has been advanced by Libman. He has made careful pathological studies of many hearts that showed extensive scarring of the valves, neighboring mural endocardium and chordæ tendineæ; no bacteria were found in the valves; Bracht-Wachter bodies but no Aschoff

¹ Oille, Graham and Detweiler: *Trans. Assn. Am. Physicians*, 1915, 30, 672. Also *ibid.*, 1924, 39, 227.

bodies were found in the heart; typical old embolic glomerular lesions were found in the kidneys. He interprets these as evidence of a preceding infection with the *Streptococcus viridans*, the valves being in a bacteria-free stage with healing. He has seen not a few cases clinically in which bacteria disappeared from the blood and the fever became less or vanished. Many of these succumbed to the exhaustion, anemia, nephritis or cardiac weakness left as the result of the preceding infection. Some patients come to the physician in the bacteria-free stage, the endocarditic condition being recognized only by the cardiac signs, the large spleen, anemia, pigmented face, nephritis and the history of tender spots, petechiae etc.¹

One must feel, therefore, that grave as is the prognosis in what we would call the well-marked typical case of subacute streptococcic endocarditis there is a better outlook than has been commonly thought. Spontaneous recovery is more frequent than has been considered. This offers more hope of recovery in the severer form if the means of assisting nature can be found.

Death in the subacute and chronic forms is frequently from progressive exhaustion. Anemia, insufficient food, faulty digestion and elimination, loss of sleep, and prolonged toxemia gradually wear the patient out. Some die of nephritis, others have pericarditis or pleurisy as contributing factors; not a few succumb to embolic accidents, *e. g.*, cerebral embolism. Some die of heart failure with the ordinary signs of myocardial failure. Some succumb to intercurrent diseases as pneumonia or tuberculosis or to some disease unconnected with the endocarditis.

Treatment.—When the outlook is so unpromising one might feel that treatment is useless. This is especially true of the acuter cases. But the physician should feel that the case in hand may be one of the exceptional ones in which recovery may ensue. It is his duty to treat annoying symptoms and to alleviate suffering, details of which need not be given. The chronic patients are sometimes hard to handle in that they demur at keeping quiet and at times it seems an unnecessary hardship to make them stay in bed constantly. Comparative rest is, however, wise as it conserves the heart's strength, lessens the danger of emboli and improves the prospect of spontaneous recovery.

Unfortunately there is no specific treatment. Vaccines and sera of various kinds have proved of no value. The same must be said of the silver salts, nuclein, and a long array of drugs. To satisfy the friends they are often employed but it is wrong to hold out more than a faint hope of any good coming from them. The proof that has been brought forward showing that some of the milder cases may recover should encourage us to persist in all efforts to conserve the patient's strength and to improve his resisting power. The success of Capps with several cases, even though of milder form, is a warrant for further trial of his method of using cacodylate of sodium. He gives for many weeks or months daily doses intravenously of from 1 to 5 gr., the average being 3 gr. Care should be taken that a reliable preparation of the drug is obtained. It

¹Libman: Prognosis in Subacute Bacterial Endocarditis, *Am. Heart Jour.*, 1925, 1, 25.

is better to make up a fresh solution about every week. Mercurochrome and gentian violet, recently advocated, will probably go the way of other drugs once viewed so hopefully. Yet search for some chemotherapeutic agent should be continued.

In a disease such as the acute form, in which the organism, the pathological changes and the clinical manifestations are so well known, there would seem to be promise of relief from specific sera or vaccines. Such relief, however, has not been forthcoming. Several workers have immunized animals, including man, against the *Streptococcus viridans* and have employed the immune serum or the immune blood in treatment. No permanent favorable results have been obtained. Many lives might be saved if the sufferers from chronic rheumatic valvular defects could receive some protective inoculation against the *Streptococcus viridans*. The best preventive would be the annihilation of rheumatic fever, which by damaging valves makes fertile the soil on which develops the later serious disease. To this end attention should be paid to the prophylactic measures mentioned in discussing the simple form of endocarditis.

CHAPTER] XVII

HYPERTROPHY OF THE HEART

[BY ALEXANDER G. GIBSON, M.D., F.R.C.P.

GENERAL CONSIDERATIONS.

Introductory.—Hypertrophy, a property possessed by most organs of increasing in bulk, and allied in the lower forms of life to the function of reproducing lost parts, is in the higher forms restricted to the production of a greater capacity for total work in particular organs by increase of tissue. Under the general term is included hyperplasia, an increase in the number of normal cells, and true hypertrophy, which is an increase in the size of the cells themselves. In the following pages the term will be restricted to its more general meaning, for we are not yet able to specify to what extent the two processes participate in hypertrophy of the heart muscle. It is true to say, however, that whereas hyperplasia is more frequent in the milder and more permanent degrees of hypertrophy the grosser and active forms always show enlargement of the fibres.

Taking the single cell, we do not know how this process of hypertrophy is effected, and, indeed, a purely theoretical question such as this need not concern us. From the stand-point of the organ and of the organism, however, its conditions are better known, as definite anatomical features accompany equally definite circumstances, and from a study of such it is possible to form some notion of the stimuli by which it is called forth. Let us therefore attempt to answer the question, *What is the immediate stimulus to hypertrophy?*

From the fact that hypertrophy of an organ is invariably accompanied by an increase in its activity and, conversely, that any increase in activity if persisted in over a moderate time is followed by hypertrophy, it is probably true that the two processes are bound up with one another; it might even be said that hypertrophy is the anatomical expression of the increased activity. Just as the contraction of a muscle becomes the indirect expression of the activity of a nerve, so it is legitimate to infer that an increase in activity will be followed by hypertrophy; hence, if the conditions of increased activity of heart muscle are inquired into, stimuli will be found which give rise to hypertrophy. Heart muscle can be stimulated directly or indirectly by means of nerves, and the direct stimuli are mechanical, chemical, thermal, and electrical; the mechanical, chemical, and nervous stimuli concern us here.

Mechanical.—Such stimuli may be of various kinds, but that which concerns us here is mechanical stretching or an increased resistance to contraction.

In skeletal muscle it is well known that stretching, especially sudden stretching, can stimulate sufficiently to cause a contraction. Fick's

law is that a muscle elicits more or less work according to the degree to which it is stretched and in the heart there is a direct proportion between the diastolic volume and the energy set free in the following systole; the amount of blood therefore received by the heart may vary within very wide limits and the output will be the same as the intake.¹ The presence of an increased amount of urine in the bladder is associated with an increase in the rhythmical contractions of that organ. In the snail's heart contractions stop if the chambers are emptied by bleeding and begin again if pressure be again put into the system. Von Frey² showed experimentally that an increase of resistance acts as a stimulus to the frog's heart and the amount of distention regulates the force expended in the beat. The time relations are too quick to allow of its being due to a reflex regulating mechanism, for the increase in force with an increase in distention often appears in the systole immediately following. Moreover, the mechanism is still present after the severance of all nerves (Rieder³). Of the relation of muscular volume to resistance, the conditions of the fetal heart are instructive and conclusive; Gibson and Gillespie⁴ showed that before birth the walls of the ventricles of the heart are of equal thickness; after birth, when the two cavities are entirely cut off from one another directly, the right ventricle increases in thickness at a much slower rate than the left. In fetal life the pressure in the two ventricles is approximately equal from the patency of the ductus arteriosus; after birth, when the umbilical artery is closed, the pressure in the right auricle immediately falls, the valve of Vieussens closes, and the ventricle requires no more, if as much, force to propel the blood to the left auricle through the lungs.

Chemical.—That a chemical substance circulating in the blood can increase the activity of muscle and cause it to increase in volume is probably true, but full proof is wanting. Of the substances to be thought of in this connection are veratrin, digitalis, epinephrine, pituitrin and the cardiac tonics. A chemical element, again, may be present in renal disease or Graves' disease where heart changes occur, but the hypothesis of a chemical stimulus to heart activity in these diseases is as yet unproved; very significant is the fact that renal disease with hypertrophy is always associated with hypertrophy of the suprarenal glands and sometimes with abnormality of the pituitary body. From the cardiac hypertrophy that occurs in acromegaly it can be inferred that the secretion of the pituitary gland is the factor concerned.⁵ Pressor substances can be demonstrated in the tissue juices and urine.

Nervous.—Muscular tissue can be stimulated to increased activity by nervous action. In heart muscle there is little direct proof of hypertrophy following increased stimuli, because if we take the myogenic hypothesis as correct, the nerves of the heart have only a secondary effect in altering the muscle action. But considering skeletal muscle,

¹ Patterson, Piper and Starling: *Jour. Physiol. Camb.*, 1914, **48**, 465.

² *Deutsch. Arch. f. klin. Med.*, 1890, **48**, 398.

³ *Deutsch. Arch. f. klin. Med.*, 1895; quoted by Thorel in *Lubarsch und Ostertag's Ergebnisse der Pathologie*, 1904, p. 797.

⁴ *Edinburgh Medical Journal*, 1892, **38**, 429.

⁵ Humphrey and Dixon: *Brit. Med. Jour.*, 1910, ii, 1047.

ample proof is not wanting. If a nerve to a skeletal muscle be cut the latter degenerates, while if the nerves be more frequently stimulated, as by electricity or by use, the muscle hypertrophies. In regard to the relation of nervous action to cardiac hypertrophy only indirect evidence is available. Hering found that if the heart is in standstill, stimulation of the sympathetic nerve supply will cause the heart to beat; it has long been known that stimulation of the sympathetic nerves to the heart will produce a faster rate and a more powerful contraction than in the normal condition. A few clinical conditions point to this cause as the origin of conditions of hypertrophy. In neuritic lesions of the brachial plexus, especially the left side, it is not unusual to find evidence of some hypertrophy of the heart (Potain). The slight hypertrophy met with in neurotic persons is probably of this nature. Moreover, such may be the cause of the hypertrophy found in Graves' disease, as a result of excessive sexual indulgence and that sometimes associated with growth.

Nutrition and Hypertrophy.—The relation between hypertrophy and hyperemia is very close, and in heart muscle probably plays a very essential part in the ultimate establishment of that process. Instances in general pathology of hyperemia causing hypertrophy are sufficiently numerous, as, for instance, after cutting the cervical sympathetic nerve on one side of the neck of a rabbit a more vigorous growth of hair on that side results. In skeletal muscles the sequence of events is probably this: increased activity of muscle from stimuli arising from motor nerves, increased contraction of muscle, afferent impulses then travel up and reflexly cause dilatation of the muscular arterioles, and the increased nourishment thus supplied causes a direct increase in the size and probably the number of the muscle fibres. By analogy the same process may occur in the heart; the increased contraction may be brought about by any one of the conditions enumerated; this causes reflexly a hyperemia of the muscle and consequently hypertrophy of the muscle fibres. Or another possibility is that the increase in aortic pressure produced by an increase in heart activity forces more blood into the coronary arteries. Albrecht,¹ from an examination of hearts in which hypertrophy was present, strongly advocated the view that hypertrophy is a true inflammatory process or a proliferating myocarditis. He found changes of the nature of hypertrophy in the neighborhood of undoubted foci of inflammation. But it may be doubted whether Albrecht's view expresses more than a portion of the truth. If it be true that hyperemia in heart muscle produces hypertrophy, then hyperemia, whether general, as from reflex nervous processes, or local, as from a small inflammatory focus, will cause the muscle to react in the same manner in either case. Moreover, other authors² have not been able to confirm Albrecht's proposition that in hearts, *e. g.*, from cases of hypertrophy from renal disease, there are foci of inflammation, unless produced by an accompanying sclerosis of the coronary vessels. Krehl is of the opinion that increased nutriment of itself does not lead to hypertrophy of the heart, except when it is associated with an increase of activity, for an increased pressure in the coro-

¹ *Der Herzmuskel*, Berlin, 1903.

² See Aschoff and Tawara, *Grundlagen der Herzschwäche*, Jena, 1906.

nary arteries does not necessarily lead to hypertrophy of the right ventricle (*e. g.*, in renal disease); but it has been determined that the area of dogs' hearts as shown by the orthodiagraph increases with an increase of diet.

That hypertrophy is not dependent on adequate general nutrition was proved by Tangl, who, after producing an artificial insufficiency of the aortic valves in starving dogs, still found hypertrophy to occur.

HYPERTROPHY AS OCCURRING IN A NORMAL HEART

The Relation between Muscular Work and Hypertrophy.—A number of conditions of life, chiefly those associated with muscular exertion, lead ultimately to hypertrophy of the heart. As Clifford Allbutt pointed out in 1870, many laborious occupations lead to marked hypertrophy and cardiac failure. When muscular work interferes with function it would be classed under cardiac insufficiency but we are justified in thinking, from the results of certain observations, unfortunately by no means complete as proof, that increased muscular work, when carried out under conditions which are within the physiological limits for the particular person, leads to a certain amount of cardiac hypertrophy—an hypertrophy which is associated with the necessity for a widening of the amplitude of cardiac response, for the setting free of many times the energy that is given forth at rest. This property of the heart to be able to accomplish more than it has done at rest is called reserve power. The normal heart, when the body is at rest, does an amount of work which is determined by certain internal needs of the body, by far the most important of which is an adequate supply of blood to the skin to balance the heat lost by cooling.

In this relation it is absurd to suppose that an hypertrophied heart, that only possesses a greater breadth of reserve power than the non-hypertrophied, does more work at rest than corresponds to the needs of the body. The heart hypertrophied as the result of work differs from the normal heart in that it possesses a much greater amplitude of reserve power, *i. e.*, the demand which can be put on the hypertrophied heart because of its breadth of reserve power is many times greater than in ordinary hearts. But it is doubtful if all increase in the reserve power means an increase in heart muscle; certain experiments of the writer show that an increase in hemoglobin and possibly some lessening of blood volume occur long before any hypertrophy is evident; in fact, clinically and to roentgen-rays, the hearts of athletes engaged in ordinary contests, such as football and rowing, are not enlarged. This has been recently confirmed by the careful observations of Gordon, Levine and Wilmaers¹ on Marathon runners.

Kulbs² found an increase in the weight of the heart in proportion to the degree of work performed. He took two pairs of dogs, the dogs in each pair being as nearly similar as possible in weight, build, and age. He then subjected them to similar conditions, except that one of each pair was made to do work on an endless stage. In both experiments there

¹ *Arch. Int. Med.*, 1924, **33**, 425.

² *Archiv. f. experim. Path. u. Pharm.*, 1906, **55**, 288.

was a marked increase in the weight of the heart in the animal that had done work. Thus the relation of heart muscle to skeletal muscle in the controls was respectively 1 to 53.9 and 1 to 59, and in the animals subjected to work 1 to 37.4 and 1 to 37.7 respectively—a proportion exactly that of the relation of the heart muscle to skeletal muscle in the deer. The increase affected the right as well as the left side. But the increase of heart muscle was much greater in proportion than that of the skeletal muscle. Thus in one pair the increase in heart weight was 53 gm. from 99 gm. (the weight of the control animal's heart) and the increase in skeletal musculature was 354 gm. from 5342 gm. (the weight of the control animal's musculature). If the skeletal musculature had increased in the same proportion as that of the heart it should have been 8201 instead of 5696 gm. in the working animal of the first pair

FIG. 30.

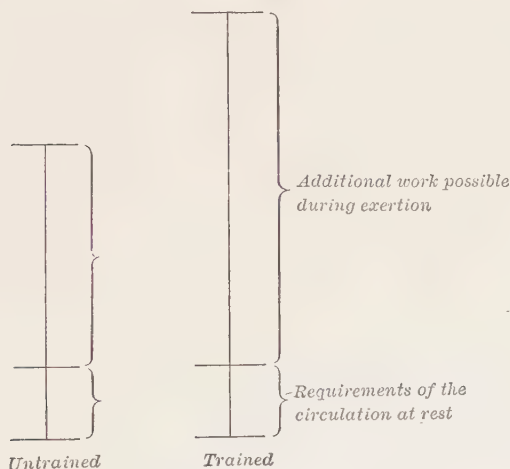


Diagram to show the difference between the heart of an untrained person and a trained athlete.

and 10,313 instead of 6498 in that of the second pair. There was a marked increase in the weight of the liver, spleen, kidneys, lungs, and pancreas, especially the first; it is therefore possible that the increase in work of these organs from metabolic reasons requires a further increase in the heart weight.

Grober¹ weighed the total heart and its parts of rabbits in confinement, wild rabbits, and hares, and found a much heavier heart in the wild rabbits than in the tame and in the hares than in the wild rabbits. This order corresponds with the degree of their muscular activity. The enlargement affects the right side of the heart more than the left; thus, in one instance quoted the left ventricle of the tame rabbit weighed 0.989 gm. while that of the hare weighed 2.840 gm., about thrice the amount; and

¹ *Deut. Arch. f. klin. Med.*, 1907, **91**, 502.

the right ventricle of the tame rabbit 0.462 gm., of the hare 1.860 gm., more than four times the amount.

When the strain of muscular work is greater than it is possible for the person to withstand, owing to the continued high pressure in the cavities of the heart, there is a failure to expel the whole of the blood brought to the ventricle; the consequence is a *dilatation* of one or more of the cavities of the heart for the time and an interference with the proper action of the cardiac muscle. In such a person at rest, in order to expel the necessary amount of blood into the aorta, the heart at each systole would have to exert, by reason of the dilatation of its cavity, a greater pressure per unit area of its internal surface than a heart whose cavity was not so dilated. The amount of work expended at rest in such a heart per unit of time would be greater than in the normal heart.

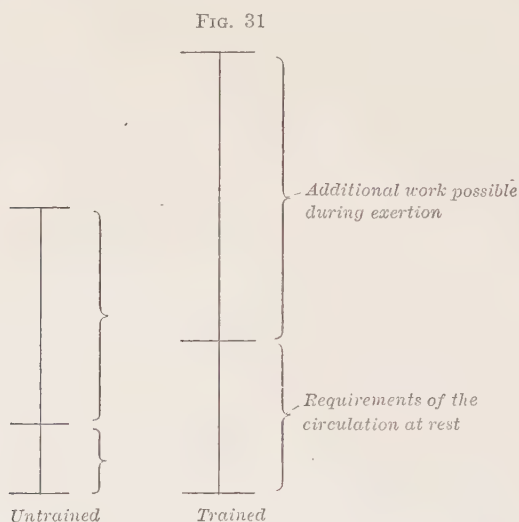


Diagram to show the difference between the heart of an untrained person and an athlete whose heart is beginning to enlarge as the result of overstrain.

We may conclude therefore that physiologically an increase of muscle can occur in the heart as the result of muscular work. This is evident from the rough test that a man's heart is the same size as his fist. The onset of hypertrophy in an athlete, however, is frequently accompanied by symptoms at rest and it is desirable under these circumstances to inquire if there has been any recent infection or ill health. It has been said that athletes' hearts are not increased in size and the rule is to look upon such hypertrophy as abnormal. The distinction of most value, if it can be made, is whether the work of the heart during rest of the body is increased or not.

In this section it is desirable to treat only of those conditions in which there is no reason to suspect an increase of heart requirements during rest. The conditions under which normal hypertrophy occurs are:

1. The so-called hypertrophy of growth.
2. The hypertrophy of exertion.

1. **The So-called Hypertrophy of Growth.**—It has been asserted, especially by French writers, that children and young people about the age of puberty frequently show both objective and subjective signs pointing to hypertrophy of the heart. Judging from the published accounts of the cases, the condition is one with occasionally some enlargement of the heart, especially to the right, and with increased force of the beat, as felt in the chest. We require, therefore, further evidence on the point whether the heart at rest is acting with more power but as a phenomenon seen in children with no suspicion of disease, it is well to insert it at this stage, and not leave it to be included among the abnormal causes of hypertrophy.

2. **The Hypertrophy of Exertion.**—This form has been made known to us by observations on a certain type of athlete, viz., those who use ski or cycles constantly. It has been noticed that in the Marathon runner and in all forms of sport requiring great exertion for a short time hypertrophy is not caused in normally trained persons. The difference in those examples of hypertrophy now to be considered is that the exertion is much more prolonged and constant. That such hypertrophy is physiological has been confirmed by a disappearance of the hypertrophy with the return to a life of less exertion.

The use of *ski* for locomotion is attended with but ordinary exertion on even ground, but in rough or hilly regions the efforts required are maximal. Henschen determined in Laplanders the presence of hypertrophy of the heart; if not of the whole heart, yet certainly of the left ventricle. Dedichen¹ found that hypertrophy occurred only if the sport was begun before the age of twenty years.

Schieffer,² investigating by means of roentgen-rays and percussion the size of the heart in young men of the age of military service, found that habitual use of the cycle caused a definite increase in the size of the heart area. He found that even hard occasional cycling did not produce any result which could be determined by his method, but that if a cycle is used continuously for three years such evidence is always forthcoming, and if it is continued for a longer period the hypertrophy increases. Both the transverse and the longitudinal diameters of the roentgen-ray picture are increased. In 13 of 35 men who had used cycles for three to fifteen years the superficies of the heart exceeded by 25.9 sq. cm. the normal (even up to 35 sq. cm. in some). The normal areas are obtained for the corresponding heights and weights from Dietlen's³ figures. Whether the size of the heart's area is taken in proportion to the weight or height, it still shows an increased proportion from 5 to 29 per cent.

It is only right to say that Schieffer believes that there is in all these hearts examined an abnormal dilatation, and that it is an abnormal condition. He supposes, although he has no direct proof, that such persons are more in danger of heart failure than others. From one point of view, however, being otherwise normal men in a healthy condition, they can stand as much strain as other young adults. But from clinical examination, a certain number are evidently abnormal. Thus, 4 out of 71 indi-

¹ *Nordsk. Mag. for Loegeviden-Skabeen Christiania*, 1920; Abstract in *Archives des Mal. du Cœur.*, Paris, 1921.

² *Deutsch. Arch. f. klin. Med.*, 1907, 89, 604.

³ *Ibid.*, 1906, 88, 55.

viduals had an apex beat outside the nipple line, 11 had it in the nipple line, 30 almost in the nipple line, while 20 had it within. In 14 there was a systolic murmur at the apex and 44 had an accentuated pulmonary second sound. It may be doubted if all these are normal, but it is probably right to assume that a certain proportion had hearts which showed no signs of dilatation or insufficiency at rest.

The volume of the heart muscle in animals bears a definite proportion to the amount of work which the animals' habits of life necessitate. The same has been shown for human beings living in mountainous districts as compared with those living in the plains. It is well known that heart failure is much more common in very mountainous districts than in flat countries. Mosso (*Der Mensch auf den Hochalpen*) mentions this fact, and that the majority of old persons die of heart failure. The "Tubingen heart" is a classical example of heart failure the result of arduous labor in a hilly district. These facts suggest that in normal persons the heart must be heavier than in those who do no arduous daily work.

Kalmansohn¹ investigated the hearts from 379 patients not dying of heart disease or associated with any obvious cause of hypertrophy. He found that the average weight of the heart for corresponding age periods of twenty years is greater in Zurich than that obtained by Müller in Jena and Peacock in London. It affects women as well as men, but the former not so markedly—and the difference become less marked, especially in women over the age of forty years. In most of the patients no abnormality had been detected in the heart during life.

Anatomy and Histology.—We have yet to learn from actual data whether in these cases the cavity of the heart is enlarged or not, whether such hearts are to be looked upon as concentrically or excentrically hypertrophied. Moritz conceives it impossible to have an increase in the size of the fibres of the heart wall without a corresponding increase in the internal surface; but the very fact of there being a concentric hypertrophy in the new-born child and in children up to the tenth year² suggests that an increase in growth is not necessarily associated with an increase in the size of the heart cavities. On the other hand, if we suppose that the tonicity of heart muscle is variable, it is probably true to say that when heart tonicity is great the muscular walls are well knit together and the cavities smaller, in the same manner as, for instance, in rigor, than when tonicity is at a lower level. Further work is required to give more insight into these conditions, and all we can suppose at present is that in the hypertrophy of work new relations are set up in the heart, which, with an increase in the bulk of its muscle, put no additional burden on the mechanism when the person is at rest.

So little is known of the conditions that exist in man that what knowledge is available is derived from the study of the hearts of animals under experimental conditions. Külbs, in dogs which have been subjected to work compared with dogs not so treated, found the heart increased in size as a whole and showing an increased thickness of the walls of the left ventricle, right ventricle, and ventricular septum (Fig. 32).

¹ *Diss. zur Herzgewicht*, Zurich, 1897.

² Parrot, quoted by Thorel, *Ergebnisse der Pathologie*, 1903, p. 759.

Grober found that the right ventricle is increased more than the left, and mentions that in the animals of active habit the parts not weighed

FIG. 32



Heart of normal dog, 99 gm.

Heart of dog subjected to work, 152 gm.

FIG. 33

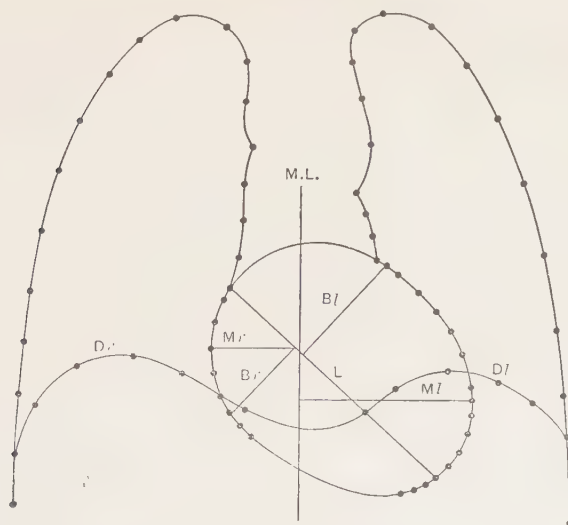


Diagram to show the method of measuring an orthodiagram of the heart: *L*, long diameter; *Br*, *Bl*, breadth to right and left sides respectively; *Mr*, *Ml*, breadth to right and left respectively, taken in the horizontal direction; *ML*, middle line; *Dr*, *Dl* = right and left sides of the diaphragm respectively. The dotted line shows the lines which are marked in at the time of taking the orthodiagram. (After Dietlen.)

(auricles) appear to be increased in proportion to the others. Owing to technical difficulties, nothing certain is known of the size of the cavities of the heart.

Histologically such hearts are sharply marked off from hearts hypertrophied as the result of a valvular lesion. The fibres are not increased in size, nor do they show an increase in the amount of sarcoplasm. An increase of interstitial tissue is not present.

Diagnosis.—Ex hypothesi we have defined this type of hypertrophy as one which is developed only for special times during the period of exertion. Symptoms are therefore out of the question except during the period of exertion at the limits of cardiac endurance. Further, many of the usual signs of hypertrophy, increased power of the apex beat and accentuated second sound at the base, are probably not evidence of hypertrophy so much as of the overaction which is necessary even during rest to combat the effects of interference against which the hypertrophy is the normal reaction. We arrive, therefore, at the opinion that a heart which at rest gives signs such as a heaving or diffuse apex beat, with a strong pulse and accentuated second sound, is one which is less efficient than one in which the apex is localized and not forcible, with no marked increase in pulse volume and with no accentuated second sound. In other words, a hypertrophied heart which is doing more work at rest than a normal heart is one which cannot run the same risk as one which does not show such signs.

With the use of the roentgen-rays it is possible to estimate with considerable accuracy the size of the outline of the heart as shown on the screen. Dietlen¹ recorded his observations on the size of the normal heart by means of the orthodiagram, at the same time comparing with this the results of percussion. The examinations were made on 187 men and 74 women, all free from cardiac or severe skeletal disease. He finds that the size of the heart varies somewhat with the height, but a much more constant relation exists between the weight and the size of the heart area; that the mammillary line bears no fixed relation to the height or weight, varying in men from 8 to 13 cm. from the mid-line; therefore, information as regards the apex beat made with reference to the nipple line is not of much value. The size of the heart increases with age. The apex beat is generally felt in the intercostal space above that in which by the roentgen-rays the apex is thought to be.

Percussion of the heart in the hands of men who have tested their results by means of roentgen-rays appears to give highly accurate results except in one or two conditions, such as emphysema of the lungs. No special form of percussion seems to give more accurate results than another. Every physician develops his own method of percussion and comparing one patient with another considerable accuracy may be attained. There is not the same accuracy when one man's results are compared with another. Such comparisons do not, however, detract from the essential value of the method in skilled hands. Hermann and Wilson² conclude that the weight of the ventricle is only one of many factors which may alter the electrocardiogram; it is therefore not to be relied on as indicating hypertrophy.

¹ *Deutsch. Arch. f. klin. Med.*, 1906–1907, **88**, 55 and 286; see also Simons (p. 246) and Moritz (p. 277).

² *Heart*, London, 1921–1922, **9**, 91.

HYPERTROPHY AS A DEFENCE AGAINST A PATHOLOGICAL CONDITION

The hypertrophy previously discussed has been such as only served to increase the total activity of the heart at certain times; we have now to examine the conditions under which for the proper upkeep of the circulation a constant increase in heart work is required. Broadly speaking, the one cause of such necessity is *an increase in the residual blood in the heart chambers after systole*; such an extra amount of blood, together with that which flows in during the diastole, requires a larger cavity at the beginning of systole than formerly. In order to effect the required transference of blood into the next chamber or tube the same pressure must be communicated to the liquid as before, this being given to the liquid

FIG. 34

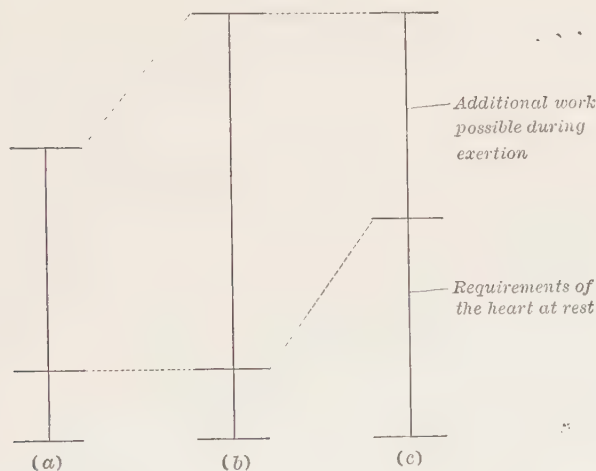


Diagram to represent the three stages of hypertrophy: *a* is a normal heart; *b* is that due to certain arduous occupations; *c* is a heart which has undergone compensatory dilatation and consequent hypertrophy.

by the contraction of the walls of the cavity. But in order for the amount of blood to be at the same pressure as formerly the same pressure per unit area of the internal surface of the cavity must be given as before; hence, if the internal surface is greater the total required is greater and the heart must beat more strongly. But an increased activity when continued leads to hypertrophy. Such an example would apply to the conditions occurring after a lesion to a valve or a dilatation of the heart the result of a strain. If the lesion causes a permanent increase in the residual or diastolic blood in the heart, then the cavity of the heart is permanently enlarged and the hypertrophy which develops is probably also permanent. The dilatation would then be spoken of as *compensatory*, and although when compensatory dilatation becomes great, it may merge gradually into the dilatation associated with and accompanying some

forms of chronic cardiac insufficiency, in the forms with which we are here dealing, in which the circulation is compensated for rest, it must be clearly distinguished from heart failure.

The accompanying diagram represents the conditions of the heart in three stages: *a* is a normal heart; *b* a heart with an increase of reserve power, such as a heart hypertrophied as the result of muscular exertion, and *c* is a heart which has undergone compensatory dilatation and consequent hypertrophy.

Etiology.—1. **From an Interference with the Heart as a Contracting Organ.**—(*a*) *Overexertion* has long been known as a cause of hypertrophy beyond the limits of the normal heart, and is fully recognized as a very important cause of non-valvular disorder of the heart. We have no reason to suppose that in the majority of cases any other factor is concerned than the strain on the heart due to the exertion, although in some cases other factors, such as a previous infection or alcohol play, a part. It matters not to what class a person belongs, any prolonged or very arduous exertion will sooner or later lead over and above an hypertrophy of work to an hypertrophy which is also associated with compensatory dilatation. We lack sure evidence of the extent to which hypertrophy coming on in foundrymen, hammermen, and others in early middle life is not to some extent due to alcohol or syphilis. The same suspicion can hardly be entertained with regard to the majority of men engaged in college athletic sports, many of whom, from their school-days, have led very careful lives. Even in these, however, we cannot eliminate the effect of a previous infection, an attack of diphtheria or pneumonia, which would detract from the total capacity of the heart muscles in accommodating itself to exertion. Certain families are notably long-lived, probably, in chief part, because of particularly good cardiac muscle. Such hereditary endowments, upon whatever they depend, can hardly fail to influence the degree to which muscular work can be pushed without causing hypertrophy. As an example of marked hypertrophy from overexertion the following case may be cited: An undergraduate, aged twenty years, while rowing in his college boat, showed signs of ill health and was advised not to row any more; he was examined by a London consultant and pronounced to have “two murmurs,” according to the patient’s account of himself. He was advised to take life easily and avoid any overexertion. About six months later he was seen while suffering from an attack of influenza and, being told of his heart condition, the writer examined his heart carefully and could find no sign of any cardiac disease as he lay in bed; his apex beat was well within the nipple line, the sounds were clear, and there was nothing to suggest any abnormality. Seven months later he complained of giddiness and some palpitation, coming on at night after playing tennis. In the upright position his apex beat was in the sixth interspace, $\frac{1}{2}$ inch outside the nipple line, fairly localized and forcible; there was pulsation in the fifth space and in the epigastrium. There was no dilatation of or marked pulsation in the veins of the neck. On auscultation there was a definite systolic murmur at the apex traceable a short distance toward the axilla. The second sound at the apex was reduplicated. At the base there was a well-marked systolic

murmur not heard in the vessels of the neck or below the region of the valves. No history of any infection could be elicited, and he was a person of excellent habits of life.

Hypertrophy may affect chiefly the left or the right side, and there are intermediate cases in which both sides are equally affected. Such differences are probably to be attributed to the position of the resistance which is placed in the circulation. If the obstruction is chiefly in the systemic system, we would expect the left heart to hypertrophy; if the work required great and prolonged fixation of the walls of the thorax, the obstruction to lung circulation through increased pressure in the alveoli would most affect the right side of the heart.

(b) *Hypertrophy as the Result of a Valvular Lesion.*—This is discussed in the articles dealing with the different valvular lesions.

(c) *Hypertrophy from an Obstruction to the Circulation in the Efferent Vessels from the Heart.*—The chamber which pumps blood toward the obstruction tends to be incompletely emptied owing to a diminished onflow in the arteries; the incomplete emptying produces additional stretching of the chamber walls, greater pressure in diastole, and subsequent hypertrophy. The conditions in this section group themselves into those which cause hypertrophy of the right and those which cause hypertrophy of the left side of the heart. Of the former we have emphysema, chronic bronchitis, dilatation of the bronchi, asthma, fibrosis of the lung, lesions of the left side of the heart, and sclerosis of the pulmonary artery. In these a marked epigastric pulsation and an enlargement of the dulness well outside the normal limits are of frequent occurrence.

Lichtheim showed that if the sectional area of the pulmonary circulation be lessened to one-fourth of the normal, hypertrophy of the right ventricle of the heart follows. Hirsch showed that the degree of hypertrophy in the right heart in emphysema is proportional to the extent of the change in the lungs. The left ventricle under such conditions is of normal weight or slightly under normal. In pulmonary tuberculosis, even with great fibroid change, hypertrophy of the right ventricle is rare, and when present bears no intimate relation with the degree of lung disease. Hirsch¹ showed that the hearts of persons dying from pulmonary tuberculosis are smaller than normal; hence the two factors would tend to neutralize one another.

Cases of right-sided hypertrophy of the heart occur as a result of sclerosis of the lung arteries (Ayerza's disease). Leonard Rogers described a number of cases probably syphilitic in origin among natives in India.² This is frequent in anthracosis and in those dying in pauper asylums, and is wholly distinct from changes in the lung arteries the result of mitral disease. Right-sided cardiac hypertrophy has been reported in dwellers in high attitudes and in whooping cough.

With a lesion of the *left side* of the heart, *e. g.*, mitral regurgitation or mitral stenosis, the left auricle sooner or later is unable to accommodate the extra blood which it receives, the lung system becomes overfull, and this again reacts on the right side of the heart, being the stimulus

¹ *Arch. f. klin. Med.*, 1899, **64**, 596.

² Leonard Rogers, *Quart. Jour. Med.*, Oxford, 1908-1909, **2**, 1.

for greater pressure in order to drive forward the necessary amount of blood; hence the hypertrophy of the right ventricle.

Hypertrophy of the Left Ventricle.—Arteriosclerosis of the systemic arteries has long been known to be associated with hypertrophied heart, but not in all cases does arteriosclerosis even of a marked grade lead to such changes. Affections of two portions of the arterial system are to be taken into account; one is arteriosclerosis of the aorta and the other is arteriosclerosis of the splanchnic vessels.

It has been asserted and taught that arteriosclerosis which causes dilatation of the aorta leads to hypertrophy. The dilated aorta of the sclerotic type is mainly due to syphilis; now aneurism is an extreme degree of dilation and if mere dilatation could produce hypertrophy it should be invariable in this condition. The very complete series of cases collected by Calvert¹ proves that aneurism in itself produces no hypertrophy unless the dilatation affects the aortic ring and produces dilatation. In large arterio-venous aneurisms hypertrophy has been recorded.

The hypertrophy of the heart which with such constancy accompanies renal disease of the chronic interstitial form may in a large number of cases be due to a sclerosis of the splanchnic area, as suggested by Hasenfeld. Such, however, can hardly account for cases of hypertension in renal disease twenty-four hours after the onset and leading to hypertrophy. There is agreement that the hypertrophy of the heart is secondary to the renal disease and is most frequent and most marked in chronic interstitial nephritis. There are no forms of heart special to particular forms of kidney affection. Sometimes the right ventricle as well as the left is hypertrophied; this is explained as being due to toxemia or by some as due to the coexisting chronic lung changes, by others as being due to the increased blood-pressure in the coronary arteries, and hence the increased nutriment to both chambers. According to Kirch (1924) in uncomplicated cases the left ventricle alone partakes in the hypertrophy; the right ventricle undergoes hypertrophy only after dilatation of the left.

It is not possible to decide which of the two hypotheses, the *mechanical* or the *chemical*, is the correct explanation of the production of hypertrophy. According to the first, known as Traube-Cohnheim's theory, the cutting off of a portion of a capillary system causes a rise in aortic blood-pressure. Cushing found that an increase in the pressure in the cranial cavity, until the pial vessels become blanched, causes reflexly a stimulation of the heart until the pressure has risen sufficiently to make the vessels patent again. But against this, excision of one kidney is not always followed by hypertrophy, and tying both renal arteries is not followed by an increase in aortic blood-pressure.

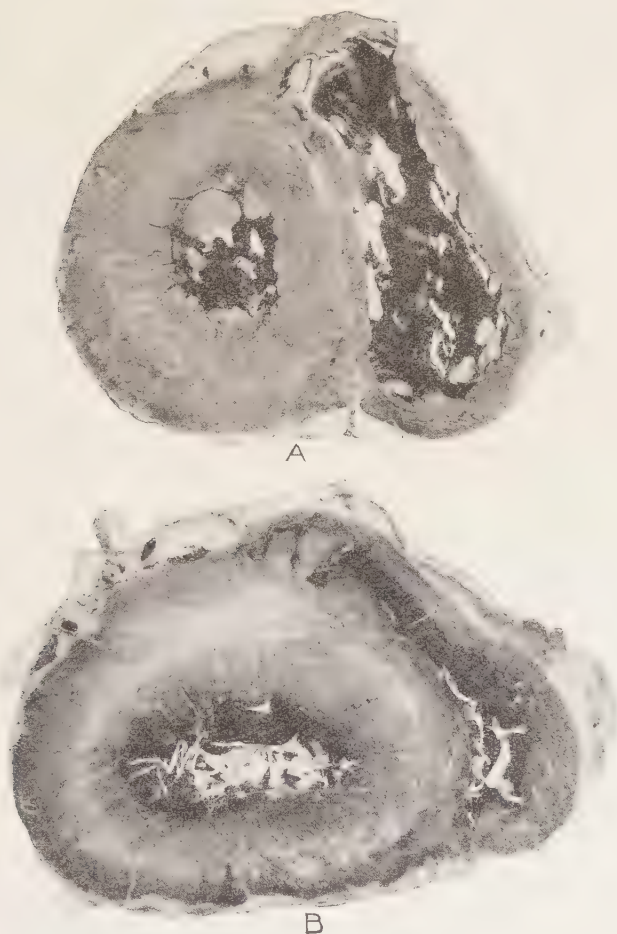
The *chemical* hypothesis of Bright, Johnson, Rosenbach, Senator, etc., supposes a failure in the excretion and a stimulation of the heart by the unexcreted material in the blood, either directly or indirectly, by causing contraction of the small bloodvessels. But hypertrophy can occur without a demonstrable excess of urinary constituents in the blood, and the injection of large quantities of urine into animals does not produce any

¹ *Medico-Chirurg. Soc. Trans.*, London, 1899, **82**, 107.

marked effect on the circulation. The viscosity of the blood is not altered sufficiently to account for the hypertrophy.

(d) *Mechanical Obstruction to Respiration*.—Any obstruction to the expansion of the chest during respiration will give rise, if long continued, to hypertrophy of the heart; just as fixation of the chest in certain bodily exercises causes some degree of right heart embarrassment, so any obstruc-

FIG. 35



A is a section of a normal heart; *B* of a heart hypertrophied as the result of renal disease.

tion to normal respiratory movement, by causing more force to be expended, gives rise to hypertrophy. It has been produced experimentally in cats. Under this section comes a right-sided hypertrophy, which has been described by Macnaughten¹ in choristers. Finley has recently described two cases in one of which there was stenosis of the aorta and in another a folding of the pulmonary artery.

¹ *Lancet*, 1905, ii, 1136.

Pleuritic Adhesions.—An association between this and right-sided heart hypertrophy has been noted. There is some other factor, however, causing the hypertrophy, for cases with few or localized adhesions may have considerable hypertrophy. In some, diaphragmatic adhesions, by which the movements of the diaphragm are impeded, give rise to considerable hypertrophy, yet the amount of hypertrophy from pleuritic adhesions is not in proportion to the extent of the diaphragmatic affection. We see many cases of extensive pleuritic adhesions with no hypertrophy.

Deformities of the chest almost invariably give rise to some hypertrophy of the right heart. It is an hypertrophy of the whole ventricular wall, and not only the conus portion, as has been supposed. No satisfactory explanation has been given of the mechanism of this form of hypertrophy; it has probably to do with the interference with lung movements or the anatomical changes consequent upon it.

(c) *From an Interference with the Heart from Without.*—*Obliteration of the Pericardial Sac.*—Two forms of obliteration from pericarditis must be distinguished: First, the cases in which the two layers of the pericardium are adherent, and, second, when, in addition to the adhesion between the two layers, there is also an extension of the cicatricial tissue to the extrapericardial tissues, thus anchoring the heart to the neighboring structures. The second type only is associated with cardiac hypertrophy. The older view, that adhesions between the heart and other resistant structures, such as the sternum, opposed a number of hindrances to the proper contraction of the ventricle and consequent propulsion of blood, has in recent years been doubted. It has been shown that the hypertrophy bears no relation to the degree of cicatricial fixation and that the synechiæ may be only slight and yet the hypertrophy may be great. It has been supposed in these cases that the hypertrophy is more probably due to other complications, such as lung changes, valvular changes or arteriosclerosis. It is impossible to say to what degree these objections are valid; certain it is that the contracting bands have some, if not the whole, effect, as witness the good results of setting free the heart from its fixation by surgical measures.

French writers describe a form of enlargement of the heart, probably of the nature of hypertrophy, which is found in patients with large abdominal tumors; the causation is not clear. It may be due to some mechanical embarrassment of the heart, a reflex irritation of the heart from the abdominal sympathetic, or a compression of the great vessels of the abdomen and a compensatory increase in aortic blood pressure, as in one explanation of the hypertrophy of renal disease.

(f) *Hypertrophy from Interference with Cardiac Muscle.*—The diseases of cardiac muscle are treated elsewhere and this aspect of hypertrophy therefore need not be considered very fully. The interferences with cardiac muscle giving rise to hypertrophy are inflammations, especially rheumatic, and myocardial changes from coronary artery disease, parasites, and new growths. Of these myocarditis and coronary artery disease produce by far the greatest hypertrophy. On the other hand, degenerations, such as fatty degeneration, are seldom associated with hypertrophy, and in the published accounts of parasites and new growths of the heart hypertrophy is negligible.

2. **Hypertrophy from Stimulation of Nerves.**—From what has been said on the immediate stimulus which causes hypertrophy, it follows that an excessive stimulation of the sympathetic nerves of the heart causing an increased rate and force of the beat might ultimately lead to hypertrophy. One of the most marked examples is that which accompanies Graves' disease. We are not able to say to what extent a direct chemical stimulation of the muscle fibres by thyroid secretion acts, but pending further knowledge we are justified in including it under this heading.

The hypertrophy which is said to result from excessive sexual indulgence is probably of this nature. Finally, there are cases in which hypertrophy appears to be due to reflex irritation of the nervous centres of the cardio-accelerator centre. Potain was the first to point out that reflex disturbances, such as dyspnoëic attacks, which were the result of chronic dyspepsia or catarrh of the bile passages, produced hypertrophy with enlargement of the right heart. This form is fully discussed by Barré.¹ Potain also drew attention to the hypertrophy which follows lesions of the brachial plexus, neuralgias, neuritides, neuroses, and neuromata, a reflex irritation and increased activity.

3. **From an Abnormal Chemical Stimulus.**—*Alcohol.* The effects of excessive beer drinking have been emphasized by Bauer and Bollinger² in their researches on the conditions of the heart in Munich autopsies. While it may be questioned whether the hypertrophy they found was due to the excess of fluid, to the alcohol, or to some other constituent, yet it is a common opinion that the alcohol alone is the harmful ingredient. This has been confirmed by finding hypertrophy among immoderate wine drinkers. Hirsch³ found in all his cases of hypertrophy from beer drinking an interstitial nephritis, which he supposes the true cause.

Various explanations have been offered for the hypertrophy. The action of the alcohol itself is a doubtful explanation, for on this it is difficult to explain the absence of hypertrophy in persons who frequently drink small quantities of spirits. Experimentally, alcohol has no power in animals to produce hypertrophy. It has been attributed, again, to the large quantity of assimilable foodstuffs in Munich beer; but this is improbable, for the reason that only certain persons are attacked. The real cause or causes are obscure, but we may conclude that there is another factor besides the beer such as, arteriosclerosis, chronic nephritis, emphysema, previous infections, or overexertion.

Tobacco.—The production of hypertrophy by this drug has been described, but the evidence of such is for the most part clinical. Both dilatation and hypertrophy have been noticed. The symptoms of poisoning are the most prominent thing, and probably a timely stoppage of its use prevents the development of hypertrophy. The chief symptoms are palpitation, coming on at rest or after slight exertion, some hyperpnoea, and occasional pain of an anginoid character.

In pituitary tumors, in which hypertrophy is sometimes noticed, we are justified in assuming that it is due to the overstimulation of the cardiac muscle by a secretion of the affected gland.

¹ *Rev. de. med.*, Paris, 1883, 3, 1.

² *Festschrift f. Pettenkofer*, München, 1893.

³ *Deutsch. Arch. f. klin. Med.*, 1900, 68, 55 and 338.

Epinephrine.—Hypertrophy from intravenous injections of epinephrine has been noticed in animals, but the appearance of the muscle which is fibrosed shows that it is irritative. In a patient with asthma given subcutaneous injections almost nightly for two years, no obvious enlargement of the heart to the left took place, no increase in blood-pressure and no thickening of the palpable arteries resulted.

Morbid Anatomy.—With the features which distinguish the muscle of hearts hypertrophied as the result of a valve lesion, dilatation of a cavity, and so forth, we are familiar. These changes consist in an increase in the volume of each fibre, an increase in the sarcoplasm, a broadening of the fibrillæ, and an increase in size and change in form of the nucleus.

Stadler,¹ from the experimental side, came to some very definite conclusions on the effects in animals from artificially produced aortic insufficiency, tricuspid insufficiency, and aortic stenosis. The changes occur in those parts of the heart on which most stress falls. The fibres are markedly increased in thickness; the sarcoplasm is much increased, sometimes to such an extent as completely to isolate the fibres. In longitudinal section the spindle-shaped space which encloses the sarcoplasm is enlarged. An increase in thickness of the fibrils is sometimes obvious, but at other times not so marked, or even at times a lessening in their thickness is evident. Many forms of nucleus are found. A most important feature in these hearts is an increase of connective tissue, showing itself sometimes as a diffuse network affecting a whole segment of the heart or a smaller area. For instance, in the right auricle, in tricuspid insufficiency, not only are the normal septa thickened, but between the single muscle fibres a more or less broad band of connective tissue has been developed. The connective tissue thus found is quite distinct from that so characteristic of myocarditis which is found in small areas. Stadler considers this increase of connective tissue as a reaction from the overfilling which acts so as to increase the elasticity of the walls of the cavity, *i. e.*, to diminish its distensibility. Opinions are less agreed on the presence of an increase of elastic tissue, some observers having found an increase, others no change. There is frequently an increase in the brown pigment at both poles of the nucleus.

The Increase of Muscle Cells in Hypertrophy.—This is by no means definitely proved. Zielonko, using frogs and rabbits in whom he made an artificial stenosis of the aorta, found an increase in the fibres of the heart. This agrees with the assertion of Kölliker, Rokitansky, Zenker, and Rindfleisch, who all suppose a splitting of the fibres to form new ones. Tangl, using the same method as Zielonko, finds that only in fetal life and shortly after birth is the muscle increased by splitting.

It is difficult to form conclusions on the extent to which in various forms of hypertrophy the muscle fibres increase in size or number. In the physiological form of hypertrophy from work the histological evidence points to no alteration in the size or appearance of the fibres; hence we must conclude that the increase in thickness is due to a larger number of normal muscle fibres being present. To suppose that physiological

hypertrophy, the muscle only doing extra work at special times, can be distinguished by the presence of normal muscular fibres, and the pathological or compensatory hypertrophy, where the muscle constantly does increased work, by an increase in the size of the fibre, alterations in the nucleus, sarcoplasm, etc., is a hypothesis for which, as yet, there is no support.

Symptoms of Compensatory Hypertrophy.—From our definition the presence of hypertrophy in itself cannot give rise to many symptoms because we have excluded all consideration of cardiac failure; nevertheless it will be advisable to mention a few, although it is difficult to say whether they are due to hypertrophy or commencing failure. Pain in the precordial region, usually of a dull type, and even true anginal attacks may occur, especially if the hypertrophy is due to disease of the coronaries or myocardial sclerosis. Various subjective sensations, such as transient giddiness, singing in the ears, or flashes of light before the eyes, may trouble the patient. On exertion, unless in well-compensated hearts with slight lesions, there may be dyspnoea.

Physical Signs of Compensatory Hypertrophy.—The appearance of the patient may present no indication; but if the hypertrophy is due to a constant high arterial pressure there may be a florid appearance and a general fulness of the tissues of the face.

Hypertrophy of the right auricle may show a more vigorous pulsation of the veins in the neck, especially when the patient is in the horizontal position; such may be more evident in a tracing. It may be possible to detect over the third and fourth ribs to the right of the sternum an impulse occurring before that of the ventricle. Dulness to the right of the sternum extends farther than normal. The contractions of the auricle normally give no sound that is loud enough to be distinguished by the ear, but when the auricle contracts more vigorously, as in hypertrophy, it may be possible to hear the auricular contraction either to the right of the sternum or over the pulsating jugular area in the neck. The *P*-wave in the electrocardiogram is larger than normal.

Hypertrophy of the right ventricle usually causes a slight bulging in the costal angle with definite *positive* pulsation, not negative as may be seen normally along the left costal border. The apex of the heart is often pushed over to the left, sometimes diffuse and never easily localized. The pulsation at the apex is usually enfeebled. The venous pulsation in the neck may be marked and the jugular pulse may be of the ventricular type. Percussion may not give any reliable evidence, but there is usually an increase of dulness to the right of the sternum from the right auricle. The first sound over the tricuspid area is loud and the pulmonary second sound is usually accentuated. The sign of enfeeblement of the right ventricle is *hyperpnœa* coming on with the least exertion.

Hypertrophy of the left auricle is not easy to diagnose. The apex tracing may show a larger wave than the auricular beat usually gives; it may again produce an audible sound, but this is uncertain, and some authors have claimed that when the left auricle is enlarged, especially in dilatation, there is dulness at the apex of the left lung. A loud pre-systolic murmur in mitral stenosis usually means, according to Mackenzie,

a vigorously acting left auricle. The *P*-wave in the electrocardiogram is larger than normal.

Hypertrophy of the *left ventricle* presents the least difficulty. On inspection there is a forcible pulsation at each heart beat, and if the patient be young, there may be some bulging of the thorax. The carotids pulsate more markedly than normally, and the apex beat, which may be in the nipple line or farther out in the fifth, sixth, or seventh spaces, is prominent and fairly easily localized. To the hand the apex beat is more forcible than normal and longer in duration. Gibson¹ described a quivering or "shuddering" sensation which is given to the hand. The first sound at the apex is louder and longer, but with some loss of compensation the sound may be short and sharp, and at the tricuspid there may be a doubling of the first sound. The aortic second sound is accentuated. The pulse is usually full and strong, or if the tension is high from renal disease, it may be hard between the beats, with strong but not large beats.

In the diagnosis of all forms of cardiac enlargement, the roentgen-rays are of great service; when the heart area can be mapped out accurately on a screen and measurement made and compared with those of the normal, such must be the final appeal in matter of enlargement. But it affords no clue whether the enlargement is due to dilatation or hypertrophy, which must be determined by the other evidence.

The Blood-pressure in Hypertrophy.—In the young athlete with a perfectly balanced circulation, it is unusual to find a high maximum or minimum blood pressure during rest; in fact, comparing young men of the same age and standing such as one finds at the universities, those who take violent exercise, as a rule, have blood pressures somewhat lower at rest than those whose pursuits are more sedentary. During exercise the blood pressure rises considerably at first, but later on, with the onset of cutaneous hyperemia and perspiration, the minimum blood pressure is often found below normal. The records of the blood pressure in cases in which hypertrophy is the result of an abnormal condition are different. The cause here, whether nephritis, a valvular lesion, an over-strain, etc., instead of being intermittent, as in the athlete, is constant; the heart has continually to do more work and, as a consequence, if there is good compensation, the blood-pressure is higher than normal.

When such an hypertrophied heart begins to fail the blood pressure may fall, but the height of the blood pressure is no evidence of the condition of the patient, for a patient whose blood pressure had dropped to 150 mm. from 200 mm. would be in a much worse plight than one whose blood pressure dropped to 120 mm. from 150 mm.

¹ *Diseases of the Heart and Aorta*, Edinburgh, 1898, p. 743.

CHAPTER XVIII

INSUFFICIENCY AND DILATATION OF THE HEART

By ALEXANDER G. GIBSON, M.D., F.R.C.P.

Theoretical.—Cardiac insufficiency is produced by any interference with the heart as a whole or any of its essential parts, preventing a proper discharge of its functions.

By far the greater number of causes which give rise to cardiac failure are due either to a mechanical interference with the action of the muscle or an anatomical change in the muscle fibres themselves from intoxication, inflammations, etc. Under the first class would be included conditions of cardiac failure from valvular defects, overexertion, resistance to the flow of blood in an arterial stem, and under the second the numerous interferences with cardiac muscle such as occur from inflammations, degenerations, parasites and new growths. Such changes are entirely independent of hypertrophy, though this may occur coincidently; in fact, hypertrophy is the property which combats interference with function; as Fränzel has said, *hypertrophy is the guarantee of life*. Cardiac failure, therefore, may occur in a hypertrophied or non-hypertrophied heart. A limit should be given to the term *cardiac insufficiency* for the purposes of description, although of necessity there is no definite line of demarcation between sound and unsound hearts. A normal heart is one whose reserve power is capable of sustaining a large amount of extra exertion without damage to its structure or size. When any cardiac impairment is present such additional exertion is not possible without distress. The average person who does not take even moderate daily exercise has a lower limit of cardiac endurance than the person who is so accustomed. Another class of patient, even if he walks a yard or two, has breathlessness or some other symptom, but when reclining in bed is comfortable. In the severest type of insufficiency there are symptoms even when at rest, with œdema and orthopnoea, such as are seen in the last stages of chronic heart failure. For clinical purposes such a subdivision as has been indicated is necessary, for it gives at once the lines along which treatment should proceed. Regarded in a slightly different way, these various classes may be looked upon as having different amounts of reserve power; that one in whom symptoms are present only on the severest exertion having the most, another in whom symptoms are present even when at rest having no reserve power at all. This lack of reserve power may be brought about in two distinct ways: In one the requirements of the heart may increase even for the resting condition, such as happens when a valve undergoes increasing erosion, or when, as the result of overexertion, the cavity of the heart dilates; in the second, with a normal amount of work to do, the power of the heart to do that work steadily diminishes; this form occurs in febrile conditions, in inflammations and degenerations of the heart muscle. When seen at the bedside the two forms occur together.

For an adequate knowledge of any condition of cardiac insufficiency it is necessary to know exactly the effect of the particular agent causing the failure on each particular function of cardiac muscle. Much light has been thrown on the conditions of heart action by the application of the researches of Gaskell and Englemann on the five functions of contractility, excitability, stimulus formation (rhythmicity), conductivity, and tonicity. It is clear that when different agencies act on heart muscle, the interference with these functions is not necessarily the same in all cases, and our knowledge to be adequate should include the effect of the cause on each one of these functions. Moreover, certain parts of the heart itself have particular functions more than other parts, thus rhythmicity is most marked at the mouths of the great veins, and least in the ventricles. We know that certain forms of irregularity of heart action are connected with a failure of one or more of these functions. Thus *pulsus alternans* is associated with a failure in the function of contractility, and other conditions are associated with a loss of conductivity, such as in Stokes-Adams disease, and the irregular pulse of mitral stenosis. Auricular fibrillation, flutter and paroxysmal tachycardia are interferences in those parts of the heart whose rhythmicity dominates the other parts.

So far as can be predicted at present it is possible that cases of sudden cardiac failure may belong to a class in which the functions of contractility, excitability, or rhythmicity may be at fault. For instance, if one considers the sudden death that occurs in cases of aortic disease, it is probably due to a failure of contractility for the time being. Again, the sudden death that occurs in fatty degeneration of the heart is probably of the same nature. Accurate knowledge of these conditions is as yet not forthcoming and such suggestions are merely guesses.

We are better acquainted with conditions of interference with conductivity, because this function, at least in certain parts of the heart, is abnormally developed in certain fibres. In the matter of transference of the stimulus from auricle to ventricle the length of time between the auricular and ventricular impulses, usually one-fifth of a second, serves as a guide to the state of this function. The stimulus of each contraction begins in all probability in that part which corresponds to the sinus venosus; this stimulus can be transmitted to the auricular node either by the auricular muscle or directly by the sino-auricular bundle of muscle fibres; it may therefore be possible to distinguish between several forms of interference with conductivity. Mackenzie suggested such a one is the irregularity coming on in mitral stenosis, the dilatation of the auricle being such as to prevent muscular conduction from the great veins to the ventricle, in whose absence the rhythm is taken on by the conducting system nearer the ventricle. Tonicity, again, is a function which in some cases of cardiac failure is probably one of the chief factors at fault.

DILATATION OF THE HEART.

Theoretical Considerations.—The term dilatation of the heart is so firmly established, both in clinical medicine and morbid anatomy, that any description of chronic cardiac failure without a reference to it would

be incomplete. So intimately is it associated with certain forms of cardiac insufficiency that the consideration of dilatation of the organ almost usurps that of the other functions. In its clinical sense the term is applied to conditions of heart insufficiency in which the main feature is an enlargement of one or more of the cavities of the heart with an enfeeblement of function; in morbid anatomy the term is applied to any enlargement of a heart chamber. The two definitions are by no means co-extensive, for a cavity may be enlarged and yet give rise to no interference with function because a concomitant hypertrophy may be the means of making the organ again effective. Such dilatation would be compensatory, and the term cardiac insufficiency could no longer be applied to it. These cases would come under the pathological variety of hypertrophy. In the dilatation which is pathological, in that heart failure accompanies it, the cavity of the heart is enlarged to such an extent that the normal pressure per unit area, owing to stretching, cannot be communicated to the heart contents. Such a condition may be the result of two main causes: in the *first* there is a progressive or sudden dilatation of the cavity by mechanical causes in which the force of the heart remains the same, which having to act on a greater surface area is not able to give the necessary pressure to the contained blood. This condition, while it leads to stimulation of the heart muscle at first, ultimately produces, either by excessive stretching or by altered nutrition from lack of blood supply, an enfeeblement of the muscle fibres themselves and consequent loss or enfeeblement of their contractile power. The *second* is that in which, without any alteration in the mechanical conditions, an alteration in the power of resistance or elasticity of the cardiac muscle takes place, by interference with its nutrition and functions; the cavity dilates as a result of the normal pressure exerted on it.

To follow up the mechanical conditions of dilatation a little further—considering the course of events in a case of mitral regurgitation—the left auricle during systole receives back a certain volume of blood which it had previously given to the ventricle; in addition to this it receives the normal or nearly the normal amount from the pulmonary veins. This extra amount of blood is easily accommodated in the auricle by dilatation from simple stretching. This causes a stimulation of the muscle of its walls and is the stimulus for an increased force being expended at the systole of the auricle, with the result that the ventricle receives the normal amount of blood, together with the extra amount which is thrown back during systole of the ventricle. The circulation is now in a condition of equilibrium again, and supposing that no interference with the nutrition of the heart muscle occurs no loss of balance is likely to occur if the extent of the valve lesion is constant. But supposing the valvular defect increases, the balance between the force necessary to drive the total amount of blood in the auricle into the ventricle and that which it is possible for the auricle even in its stimulated and hypertrophied condition to exert is lost, and the blood accumulates in the auricle and leads to further dilatation. Under these conditions of stretching, it is not possible for the muscle fibres to receive their proper nutriment and a condition of fibrosis results.

The second series of conditions under which dilatation is produced is more obscure—namely, the dilatation that accompanies the degeneration of muscle fibres of the heart. The most marked examples of this are seen in fatty degeneration, and sometimes in the degenerations which accompany fevers, especially diphtheria. In this class would be included those interferences from inflammation of the muscle—including parasitic irritation—and from new growths. It would be most rational in this class to suppose that the normal pressure during diastole and a lessened resistance to contraction of the muscle produce the same conditions as a heightened diastolic pressure and a greater demand on the contractility of the heart do in the normal condition of the fibres.

So far we have considered dilatation of the heart from increased resistance to contraction, or increased stretching during diastole, and from lesions of the muscle itself; but there is a large class in which the dilatation depends on a direct action on one or more functions of heart muscle acting either in a chemical manner through the blood or through the nerves. Such action, we presume, is not an interference with the muscle cell as a living structure but a pure interference with certain particular functions. The function of heart muscle which in this connection would attract most notice is that of *tonicity*. Bauer,¹ in 1893, was the first to suggest that certain forms of dilatation were due to a diminution of this function, and Herz² and Gossage³ attributed certain conditions to an interference of the same. We have no method clinically of estimating the condition of tonicity, so that as yet proof of the hypothesis is some way off; yet certain considerations make it very probable that changes in tonicity may be so marked as to produce great interference with heart activity. The heart of the land tortoise (*Emys europæa*) has been shown by Fano to possess in addition to the ordinary rhythmical contractions a slowly developing and slowly subsiding contraction which, when it appears, has the ordinary contractions superimposed on it. Again, Ebstein⁴ records the observation that stimulation of an exposed non-beating heart with a point of a scalpel was followed by a relaxation of the heart and dilatation of its cavities which was succeeded by an active contraction. Gossage, in speaking of the effect on this function by drugs, considers that digitalis increases tonicity, while lactic acid diminishes it. Supposing the tonicity of heart muscle to fail, the heart wall is more flabby than normal and easily receives the inflowing blood during diastole; a normal systole of such a heart will not be sufficient to empty the cavity completely; with more forcible contractions the cavity is emptied as well as before, and the circulation is undisturbed. If from degeneration of the muscle fibres contractility cannot be increased, then dilatation and consequent enfeeblement ensues. Supposing contractility alone fails, the pressure in the aorta lessens, and if all the chambers suffer equally, less blood therefore enters the ventricle and the heart merely beats more feebly without undergoing dilatation. If both contractility

¹ *Festschrift f. Pettenkofer*, 1893.

² *Deutsch. med. Wchnschr.*, 1900, 26, 128 and 148.

³ *Lancet*, 1906, ii, 1126.

⁴ *Ergebnisse der Physiologie*, Wiesbaden, 1904, III, 2, p. 168.

and tonicity were to fail simultaneously there would be little if any dilatation. In the purely mechanical origin of dilatation, such as occurs from overexertion, both tonicity and contractility oppose themselves to dilatation until from stretching, lack of proper blood or fatigue, tonicity begins to fail. Fatigue of muscle, as is well known, is accompanied by the production of an acid reaction due to sarcolactic acid, which is potent to produce a lack of tonicity.

Taken in conjunction with what will be said on chronic cardiac failure, it is evident that dilatation of the heart cannot be taken to mean the same as cardiac insufficiency. Dilatation does no doubt accompany many forms of heart failure, but the latter is the important thing and the dilatation is merely a physical sign in the course of the ailment. It is by no means desirable, however, to do away with a term of so much significance in clinical medicine. It would be well perhaps to give a little more exactness to the term, by speaking of cases of cardiac failure with dilatation rather than of dilatation alone.

CARDIAC INSUFFICIENCY

Acute Cardiac Insufficiency.—Etiology.—(a) *Wounds of the Heart.*—These may be direct by a sharp instrument, or indirect from a crush causing a fracture, or from a crush alone. It is not necessary that the wall of the heart should be penetrated. Such cases as show only a very small wound have been examined for the presence of fatty degeneration or other abnormality of cardiac muscle without success. Experiments have been undertaken which show how difficult it is to wound the heart by blows if the pericardium is intact, whether the heart is filled or not. The extent of the rupture is in no sense proportional to the symptoms or the length of time which such a patient survives; small wounds may be fatal in a few hours and with moderately large ones the patient may survive several days. Cases are by no means rare in which the heart wounds have been stitched and the patient recovered. The heart failure caused by wounds cannot wholly be due to mechanical interference with heart action, for the degree of heart failure would then probably show some relation to the size, depth, and position of the wound.

As to the phenomenon of *fibrillation* of the heart from the analogy of animal experiment we are justified in assuming that it can occur from electrical, mechanical, and chemical stimulation. Kronecker and Schney found that by stimulation of the interventricular septum of the dog's heart at the junction between the upper and middle thirds the whole heart could be thrown into fibrillary contractions. They attributed the effect to the destruction of a coördinating centre in the septum. No proof of such a centre has ever been obtained: there is no nervous tissue in that region in greater amount than in other parts, and no stimulation of special portions of the heart where nervous tissue is known to exist or of the entering nerves themselves has been found to cause fibrillation. The two sides of the ventricular septum are the sites where the two limbs of the bundle of His diverge in their course to supply the muscle of the right

and left ventricle. It is questionable whether, from the definite localization of the point according to Kronecker, we are dealing with a lesion of this important part of the cardiac musculature. Electrical, especially faradic stimulation, and chemical stimulation, as, for instance, by perfusing the coronary arteries with a solution of potassium bromide, easily cause fibrillation. The fact that recovery can occur to some extent from all stimuli shows that the hypothesis of the destruction of a coördinating nerve centre is insufficient. Two other conditions, probably alike in their effect on cardiac muscle—namely, tying a coronary artery and the injection of suprarenal extract—are potent to cause fibrillation. The relation between fibrillation and the nutrition of the muscle is therefore close, and we may suppose, in the want of further proof, that the mechanical, chemical, and electrical stimuli cause constriction of the coronary arteries supplying special areas. Stimulation of the skin produces in certain persons a local pallor due to vasoconstriction, and the same mechanism may also be present in the cardiac muscle. But as in the skin a stimulus sometimes produces a local vasodilatation not preceded by an vasoconstriction, so there may be such differences in the heart which may explain the inconstancy in the appearance of fibrillation from certain stimuli, *e. g.*, faradization.

A great danger from heart wounds lies in the amount and rapidity of the accumulation of blood in the pericardium and probably whether such remains in the pericardium or has exit into the pleura. Certain conditions affect the bleeding: a small wound, owing to its position or smallness, may be completely occluded during systole; pressure against the sternum or thoracic wall and quick thrombus formation may limit the hemorrhage. A long period of collapse favors thrombus formation, and anything, such as overexertion, which increases the blood pressure, may prove suddenly fatal. The effusion of blood, if its amount does not interfere with the heart's action so as to cause death, and failing an infection from without, undergoes absorption to some extent; an adhesion, partial or general, of the two layers of the pericardium results.

(b) *Spontaneous Rupture*.—The question whether a sound heart ever ruptures must probably be answered in the negative. The more carefully cases of spontaneous rupture of the heart are examined, the more often definite, although perhaps minute, changes in the muscular wall, which have caused a weakening of resistance at the site of the rupture, are found. The commoner causes of such rupture are infarcts and areas of softening of the heart muscle which are caused by stoppage or partial closure of the coronary arteries, small cicatrices, myocardial abscesses, foreign bodies (needles, etc.), hydatid cysts; localized fatty degeneration, and sclerosis of the coronaries in connection with brown atrophy of the muscle have also been described.

The site of the change, whether inflammation or degeneration, is a weak spot; with the pressure during systole the area becomes stretched and, varying with the elasticity, sooner or later an aneurism appears and finally a rupture occurs. Small aneurisms of apparently little significance can often be seen on the auricles of hearts from old persons; they appear as dilated pouches in between the trabeculæ somewhere

near the auricular appendix, and the substance of the dilated portion is apparently only formed of endocardium and epicardium.

As a rule, the site of the rupture is obviously related to some underlying change in the cardiac muscle. The canal leading outward may fork and open into the pericardium by two orifices. The pericardium is usually filled with blood. The condition, according to some recent statistics, occurs most frequently in men between sixty and sixty-five years of age.

Rupture of Valves.—A number of cases of valve rupture, especially of the aortic valves, have been recorded. Such occurs most commonly in valves already slightly damaged by atheroma; and if the valve is more damaged, even slight exertion may bring on rupture. But very violent exertion in healthy men has caused rupture, as likewise explosions, sudden *aéroplane* descents and other external violence.

Rupture of the aortic valves is the most common form of rupture caused by great momentary overexertion. The onset of symptoms is very sudden and the symptoms themselves very alarming; they are those of a very severe aortic insufficiency. Insufficiency of the aortic valves coming on slowly, with progressive enlargement of the heart, is discussed elsewhere.

(c) *Rapid Effusion of Blood into the Pericardium.*—Cohnheim showed, in 1882, that an injection of oil into the pericardium caused a lowering of arterial blood pressure with an increase of that in the veins. Such fluid in the pericardium acts probably by lessening the capacity of the heart to take in fluid and thus lessens its output.

Three clinical conditions are associated with a rapid effusion of fluid into the pericardium: the bursting of a cardiac aneurism, of an hydatid cyst, or the rapid transfusion of fluid in an acute inflammation. The grade of heart failure bears no marked relation to the amount of fluid; it is more dependent on the rapidity of formation, for with a slowly formed effusion more opportunity is given for the pericardium to relax and the pressure with a given amount of fluid is not therefore so great. Cohnheim found that a pressure of 300 mm. of saturated magnesium sulphate solution could be supported in a dog.

(d) *Overexertion.*—To anyone acquainted with some of the severer tests of endurance in athletic contests symptoms of heart failure are not rare. The story of the messenger from the battlefield of Marathon who fell dead after delivering the news of victory is a good example of a severe case of sudden left heart failure ending in death. In many races men come in pale and perhaps faint or vomit immediately after finishing. Some degree of failure or rather diminution of reserve power occurs in athletes whose myocardium has been affected by an infection or who have undergone improper training. A slight dilatation, a rapid pulse and diminution of capacity for exertion are the common features.

(e) *The Presence of a Large Amount of Air in the Heart.*—Two sources have probably to be taken into account: first, air which has entered by the veins, and of these the neck veins and the uterine veins after parturition are the most important; secondly, the formation of free gas in the heart during decompression after subjection to high pressures. The first is a danger which has long been taken into account in neck

operations, especially in tracheotomy. The patient is in a condition of marked dyspnoea and the inspiratory negative pressure in the neck veins is much greater than during the normal inspiratory phase. Air, when it enters a wounded vein, goes to the right side of the heart, where it hinders the proper onflow of blood into the pulmonary artery. Oxygen, however, may be injected into the veins and may be heard impeding the circulation in the right ventricle without causing heart failure.¹ Small quantities of air in transfusions cause no symptoms. In death from this cause therefore there must be some associated cardiac weakness.

(f) *Heart Thrombi*.—The number of cases of heart failure from this cause is extraordinarily small. Pawlowski collected all the cases recorded and they only come to 25, of which 19 were in the left and 4 in the right ventricle. Such thrombi are frequently of the size of a large walnut and are often attached to some portion of the heart wall or valve; hence the name polypi. They may be the cause of death in persons with no suspected disease or in diseases such as typhoid fever.

(g) *Sudden Obliteration of a Large Section of the Lung Arteries, Pulmonary Embolism*.—Experimentally, Lichtheim found that three-quarters of the lung arteries could be tied without producing any lowering effect on the carotid blood-pressure. These experiments have been modified somewhat of late. If a young dog be used and the left pulmonary artery tied without opening the pleura, the carotid pressure falls, in one case of Landgraf's from 70 mm. to 30 mm. As with all the other causes of heart failure hitherto dealt with, the more sudden the change the greater the failure, and *vice versa*. Attacks of pulmonary embolism are observed after operations that require much dissection, after influenza, typhoid fever, childbirth or obvious thrombosis in any vein. The attack is sudden, the patient with a large embolism after a few respirations may expire with great cyanosis. In less severe cases there is precordial or substernal pain, rapid breathing, cyanosis and collapse. After an hour or so cough may develop and sputum tinged with blood may be brought up.

(h) *Sudden Interference with the Coronary Circulation*.—This is most commonly the result of atheroma, thrombosis, embolism, or a spasm of the vascular walls. Cohnheim showed that after tying a coronary artery that part of the heart supplied by the vessel went into fibrillary contractions. Thrombosis is comparatively rare. Cases of embolism are usually the result of atheroma, acute non-malignant endocarditis or malignant endocarditis. Willis² finds these lesions give rise to angina pectoris, typical and atypical, gradual myocardial failure or no definite symptoms.

(i) *Mechanical Interference with the Heart, e. g., Asphyxia*.—Sudden asphyxia occurs clinically under a number of conditions. It may occur as the result of external interference, such as strangulation, or from an obstruction, partial or complete, within the air passages, such as a foreign body in the larynx, œdema of the larynx, œdema of the lungs, or spasm of the bronchial muscular apparatus. The postmortem appearances consist in an enormous engorgement and dilatation of the right side of the heart, especially of the right auricle.

¹ Tunnicliffe and Stebbing, *Lancet*, 1916, ii, 321.

² *Amer. Jour. Med. Sci.*, 1924, **168**, 165.

The increase of carbon dioxide in the blood stimulates the cardiac, respiratory, and vasomotor centres in the medulla and the cardio-accelerator centre in the cord. In the first stages we have, therefore, a slower heart beat, although more forcible from spinal stimulation, a greater respiratory activity, and an increase in blood pressure. The more forcible inspiration increases the filling of the right heart and lung vessels, and the more forcible expiration increases the venous pressure and the emptying of the left heart. The brunt of the interference tends to fall on the right side of the heart because inspiration tends to fill it and the lung vessels, but expiration tends to empty only the left side and not the right; moreover, the walls of the right auricle and ventricle, being thinner, tend the sooner to yield to the increased internal pressure. During the first stage the most important features are the accelerator action on the heart increasing the force of the beat, the inhibitory action slowing the beat, an increased venous blood pressure, and an increased arterial pressure. During the second stage the inhibitory centre becomes fatigued, the heart is becoming dilated; hence more force is necessary to expel the contained blood; therefore, the accelerator action does not have its proper effect as it does if the right side of the heart is emptied, as can be seen clinically when a very cyanotic patient with heart failure is bled. The arterial blood becomes more and more venous, and does not properly nourish the muscle of the walls; hence another source of dilatation is present.

(j) *Interference of the Heart from Infections.*—Sudden death is by no means infrequent in the course of some of the severer infectious diseases. Perhaps the one in which it is most frequently seen is diphtheria, but sudden death may also occur in scarlet fever, typhoid fever, pneumonia, smallpox, rheumatic fever, influenza and septicemia. In some cases heart-block is responsible. In all acute infections there are changes in the heart muscle, usually of the nature of cloudy swelling and sometimes of actual myocarditis, but the myocardial changes are not always clearly related to the failure. The sudden heart failure associated with enlargement and persistence of the thymus is probably infective. Tuberculosis and syphilis are rarely the cause of cardiac failure.

(k) *Poisons.*—In this place may be mentioned heart failure as the result of certain drugs, for instance, phosphorus and pilocarpine.

(l) *Interference with the Nerves of the Heart.*—The vagus is the nerve by which the functions of the heart are restrained. We are probably justified in believing that the vagus contains groups of fibres which act on special functions. Thus, Engelmann proved that under certain circumstances a pure effect can be obtained on contractility.

We cannot, however, go further at present than to say that in cases of heart failure from nervous interference it is probably the vagus through which the stimulus is conveyed, and this may have its origin either in the peripheral terminations of the nerve (as with pilocarpine), in the nerve itself, as from a tumor in the neck, in the vagal centre, as in certain cerebral tumors, or at the peripheral end of fibres which convey afferent impulses up to the vagus centre. Probably afferent fibres ending in the vagus centre are supplied to several organs. Injuries to the abdomen

frequently produce some heart failure and injuries to the larynx are sometimes fatal. Attention has been called to the sudden death caused occasionally by thoracic paracentesis, probably from sudden and severe afferent stimulation of the vagal fibres in the lungs. Another explanation given for the rare fatal effects of artificial pneumothorax is that it is due to air embolism.

Some Types of Sudden Cardiac Insufficiency.—*Sudden Rapidly Fatal Heart Failure from Paracentesis Thoracis.*¹—A female, aged eight years, had symptoms which pointed to the presence of fluid at the base of the right lung. "On June 14 it was decided to explore the affected area, and an aspirating needle was accordingly inserted in the ninth intercostal space, one and one-half inches from the spine, for a depth of about two inches; no fluid was obtained and only a drop or two of blood. Only one puncture was made, and the whole process took about one minute. A small amount of frothy blood appeared at the mouth and nose. Immediately after the withdrawal of the needle the child was observed to have lost color, or rather to have a livid appearance, with a strong, double-convergent squint, and some rigidity of the arms. The pulse could not be felt and the heart sounds were inaudible. Breathing continued irregularly for a minute or two, the respirations being slow and gasping, then ceased. Artificial respiration, which was kept up for half an hour, was of no avail, although perhaps for five or six minutes it evoked spontaneous attempts at breathing. The pulse could not be felt after the onset of symptoms." No change was found in the heart at the postmortem examination. It is not unusual in these cases, if life is prolonged further than in that quoted, to see convulsions followed by hemiplegia.

Sudden Death from Embolism of the Pulmonary Artery.—"Male,² aged twenty-four years, with moderately severe attack of typhoid fever. In the middle of the second week a fatal termination occurred under the following circumstances: At the evening visit the patient was quite well, cheerful, and had no pain. The pulse, however, and the apex beat were intermittent without being especially weak; the intermission followed regularly after the second or third pulse beat. The pulse was 80, not reckoning the failure of beats. The patient was quiet until 11 P.M., and slept well. At this hour he awoke and passed a somewhat profuse, liquid stool without any difficulty. He also passed 15 ounces of urine. He had scarcely done this and spoken a few words, when he suddenly made a few strokes with his arms, took a few deep, snorting breaths, and after a few minutes died." A plugging of a main branch of the artery supplying the inferior lobe of the right lung was found.

Right Heart Failure.—Clifford Allbutt related the following.³ "In the summer of 1868 I began to walk in the Alps a little too soon for good training. . . . I was suddenly seized with a strange and peculiar *besoin de respirer*, accompanied by a very distressing sense of distention and pulsation in the epigastrium. On placing my hand

¹ Russell, *St. Thomas' Hospital Reports*, 1899, 28, 465; see also Capps.

² Quoted by v. Jürgenson in Nothnagel's *Specielle Pathologie u. Therapie*, 15, Band i, from Virchow.

³ *St. George's Hospital Reports*, London, 1870, 5, 29.

over my heart I felt a laboring, diffused beat all over the epigastrium. I at once opened my shirt, and ascertained by percussion that the right ventricle was very greatly dilated. I therefore threw myself at length upon the grass, with my shoulders raised, and had the satisfaction in a few minutes of finding the distention, the oppression, and the dulness recede. I was then able to rise and sit down, or even to move about on the level; but, curiously enough, the instant I began to ascend, the symptoms returned. I was therefore obliged to send K. forward and proceed myself with great caution. When I got up to the height of the inn, and had only to walk a mile or two on the level by the waterway, I ceased to suffer, as I felt no general fatigue whatever, and was able to dine well on my arrival. In the night, about 3 A.M., I was suddenly awakened by a severe and distressing palpitation in the epigastrium, with great dyspnœa; there was not, however, the same extension of dulness over the sternum. I went to the window and drew a few long respirations, which gave me ease, and I lost my ailment altogether. No doubt the pressure of a full abdomen against the diaphragm, while recumbent, had again embarrassed the overtaxed right ventricle."

Chronic Cardiac Insufficiency.—Etiology.—(a) *Lesions of the Heart Muscle.*—These include wasting from new growths or diabetes; degenerations, such as cloudy swelling, fatty degeneration, amyloid degeneration; the effects produced by infections, such as diphtheria, rheumatic fever, pneumonia, influenza, dysentery, etc.; new growths of the heart muscle itself; parasites of the heart, and coronary artery disease. But while the myocardial lesions may thus be classified the chief causes of chronic insufficiency are rheumatic myocarditis, the myocarditis associated with chronic infective and ulcerative endocarditis and more rarely with syphilis.

(b) *Lesions of Valves.*—These are described in another section.

(c) *Lesions Peripheral to the Heart Itself.*—The causes under this head group themselves naturally into two, according as the lesion lies in the pulmonary or aortic arterial tree. In dealing with hypertrophy of the heart it was mentioned that a lesion of the lungs causing an obliteration of part of the blood path in the lungs could produce hypertrophy of the right ventricle. Hypertrophy of the right ventricle is the natural reaction to a lesion opposing a proper outflow from the pulmonary artery, but if the limits of hypertrophy have been attained, or if the lesion comes on so suddenly that there is no time for hypertrophy to develop, then the ventricle must become overfilled and the contractions fail. Emphysema, bronchitis, asthma, bronchial or tracheal obstruction, sclerosis of the lungs, kyphoscoliosis, deformities of the chest, and mitral disease are the most frequent causes of right-heart failure. As in hypertrophy, the left ventricle enlarges from aortic disease, arteriosclerosis of the smaller vessels, especially in the splanchnic area, and from renal disease; all these conditions may produce cardiac failure sometimes with and sometimes without hypertrophy.

Hypertrophy of the *right ventricle* in lung disease may be adequate to carry on the circulation for some time, but when the right heart fails,

diminution of the blood flow through the lungs occurs, the blood is insufficiently oxygenated and contains more carbon dioxide than normal, and shortness of breath comes on even at rest. With every additional claim on the heart, especially the slightest exercise, the distress is increased. The feebleness of the right ventricle shows itself in a diminution of the intensity of the pulmonary second sound, cyanosis and overfilling of the systemic veins, enlargement of the liver, albuminuria and oedema. If compensation is again established, such patients may live a tolerably comfortable life if they avoid exertion of every kind; but the slightest increase in the demands on the right heart may precipitate another attack and an attack of pneumonia or bronchitis, or indeed any infection, is particularly dangerous. In some cases such a heart insufficiency is brought on without any special antecedent; here it is probable that the balance between hypertrophy and an increasing obstruction in the lung arteries is now upset by the failure of the hypertrophy.

Emphysema of the lungs, which is preëminently one of the conditions giving rise to this form of cardiac failure, also causes trouble in the left side of the heart. It is difficult to see how such can be accounted for from any effect of the lung condition; it is probably to be sought in the sclerosis of the small systemic arteries, especially those supplying the myocardium, which invariably accompanies emphysema.

The two conditions which affect the left side of the heart chiefly are so similar that they may be taken together—namely, *renal disease*, particularly the granular, contracted form, and *arteriosclerosis*, especially of the splanchnic vessels. Both are associated with a high blood-pressure in the stage when hypertrophy is adequate to carry on the circulation. As soon as this fails or some unfavorable condition affects the heart muscle, or an extra amount of exertion requires greater stress, the tension is lowered; the heart beats strongly, but not with its former vigor; the second sound in the aortic area is lessened in intensity; gallop rhythm is present, and the pulse becomes less hard, although probably greater in volume. The face, which previously perhaps was a good color, becomes paler and the patient often complains of drowsiness. With this the urine becomes less in amount; some swelling of the legs, enlargement of the liver, and disturbance of alimentary functions appear.

In the latter stages the type of heart failure differs little from that produced by left-sided valvular disease, the diagnosis indeed between the different conditions being extremely difficult.

(d) *Interference with the proper movements* of the heart, as in adherent pericardium.

(e) *Excessive Stimulation of the Heart*.—Under this title we include the heart failure from excessive exercise and the rare cases from excessive venery or worry.

We have seen that overexertion is responsible for hypertrophy of the heart and for acute cardiac failure. It is beyond doubt that persons who have to do hard manual labor often suffer from heart failure severer in type and earlier in onset than those who live a more sedentary life. Clifford Allbutt pointed out the frequency of heart failure in the Sheffield foundrymen; workers in the Cornish mines and in the Glasgow ship-

building yards have been found to suffer in like degree from overstrain. Dwellers in mountainous districts die more frequently from heart disease than those in the lowlands. But the exact value of the factor of overexertion in these cases is more difficult to fix. Not all persons suffer from overexertion even in the areas where heart affections are most common. The patients come from the hospital class, and malnutrition may be a factor. In highly populated centres the possibility of alcohol and syphilis requires careful elimination. Further, even though the former factors are not valid, a previous infection, such as rheumatic fever (even one of its slighter forms), diphtheria, pneumonia, influenza, or typhoid fever—all have their own effect in interfering with the structure of cardiac muscle at the time, and therefore lessen its reserve power later in life.

Both atheroma of the aorta and arteriosclerosis may result from the increased aortic and peripheral pressure which occurs during exertion. All drugs which produce an increase in blood-pressure produce atheroma of the aorta experimentally and, the more powerful the drug to cause to rise in arterial pressure, the more does it cause changes in the aorta, but in medicinal doses no clear evidence of this can be found.

The effects of exertion on the heart have been studied by means of the roentgen-rays. Taking healthy, athletic men, there is agreement that hard exercise for a short time is not productive of any change which can be attributed in any sense to a dilatation of a cavity. Lenhoff and Levy-Dorn¹ examined the hearts of wrestlers before and after wrestling for a period of ten to thirty minutes. They found that to percussion there was a slight increase in the heart area, but by the roentgen-rays the heart was lowered from descent of the diaphragm, and, apart from a very slight increase in the convexity of the right boundary line of the heart figure, no change could be detected.

In the forms of heart failure directly the result of *overexertion* there are several variations. Slight acute attacks may be followed by complete recovery, but even with every precaution may develop into a chronic form. The commoner types may be grouped under four headings:

1. Young men accustomed to take violent exertion and engage in competitions frequently seek advice for palpitation, occasional giddiness or faintness, and an earlier onset of dyspnoea when undergoing exertion. The apex is usually well outside the nipple line, the impulse forcible and localized, the first sound is accentuated, loud and clear, and the second sound at the aortic area is accentuated; the pulse is large and strong, and the maximum blood pressure is increased.

2. Men of the ages of thirty-five to forty-five years who have for a number of years had laborious work as foundrymen, hammermen, etc., complain of fainting attacks or occasional vomiting and palpitation after exertion. They frequently have well-developed aortic regurgitation, and it is probable that in most cases the primary effect of the exertion has been atheroma of the aorta. In these cases a large proportion may be found to have syphilis of the aorta.

3. A third type occurs in young men of the working class. They

complain of general ill-health and inability to do their ordinary work and perhaps some indigestion. They are sometimes mistaken for malingerers. On examination they are, as a rule, pale; the apex is in the nipple line, not easily localized and not forcible. There is marked epigastric pulsation. The area of dullness is increased to the right. The sounds are for the most part clear, but usually there is marked accentuation at the pulmonary aortic area. The pulse is not large or strong.

4. The fourth type is indistinguishable from a severe case of mitral regurgitation; the patient is bluish and dyspnoeic; complains of great breathlessness on exertion and swelling of the legs.

Some describe the reactions of dyspeptic states on the heart. They result in a dilatation of the cavities of the right heart, accompanied sometimes by a secondary tricuspid insufficiency with its clinical consequences. The form of attack is usually sudden and sets in with indigestion. It is almost certainly nervous in its origin.

(f) *The Action of Poisons.*—The action of *alcohol* on the heart has been mentioned under Hypertrophy. Hypertrophy of the heart is the early stage; the later stage is heart failure with some special features. The heart is affected little by any other beverage than beer, very rarely in excessive wine drinkers. The reason of this is not known; it is put down as being due to the alcohol, but this is not certain. The enormous quantity of fluid taken may be a factor and, again, many who suffer often lead arduous lives.

The cardiac affection usually comes on after the middle period of life has been passed; the patient finds that certain bodily exertions are impossible without a sensation of pressure or pain. Attacks of dyspnoea at night may trouble him. On examination the apex beat is outside its normal limits, somewhat feeble, and not easily localized. To percussion both ventricles of the heart are enlarged. The first sound is not pure at the apex, and the second over the aortic area is accentuated. The pulse is somewhat feeble, irregular, and easily quickened by exertion. Recovery from such symptoms with treatment is the rule, but usually the patient suffers from further attacks of heart failure, in one of which he dies. The symptoms are those of severe cardiac failure with considerable dilatation of the heart cavities. It is extremely difficult during the cardiac failure to exclude the possibility of renal disease for renal changes though slight are constant.

The action of *tobacco* on the heart is usually seen from smoking strong cigars or strong tobacco in short pipes. Palpitation is the first sign and may be present in numbers of smokers without causing them any inconvenience. Attacks of palpitation are not uncommon and may come on without special cause in the night or after exercise, eating, or with excitement. Pain in the region of the heart is a frequent cause for seeking advice. Faintness on exertion is sometimes present. The pulse is usually small, quick, and often irregular. The size of the heart is, as a rule, not altered, but several competent observers have noted a definite increase.¹ The action of nicotine on the heart produces ultimately coronary sclerosis;

¹ See Krehl in *Nothnagel's Spec. Path. u. Therap.*, vol. 15, Band i, 262.

it is right to say, however, that there is no unanimity of opinion as to its effect in producing cardiac failure in man.

The Thyroid Heart.—The cause of the heart changes in *Graves' disease* is by no means clear. The capacity of the heart to do work is less in *Graves' disease* than in normal persons; any slight exertion causes breathlessness and an increase in the rapidity of the pulse. Serious cardiac failure in young subjects is by no means rare; it usually comes on after a period of steady loss in weight and, in fact, a fatal termination to the disease is usually the result of cardiac failure. In the early stages if the patient has been walking about there may be found a slightly displaced apex beat, a sudden impulse, a slight increase of dulness to the left, a slapping first sound at the apex, followed sometimes by a well-marked systolic murmur, an accentuated second sound over the pulmonary area at the base, and a pulse which is large in volume but poor in tension. Later, œdema, dyspnœa, and cyanosis appear with very little increase in the size of the heart. Fibrillation in the later stages is constant. Post-mortem, the cavities of the heart are not usually much dilated, the heart muscle is pale and not markedly increased in amount. The valves are slightly thickened. These changes are seen more frequently in the so-called toxic goitre in which there may be no enlargement of the thyroid and no marked eye signs. Any serious diminution of exercise tolerance, such as these patients show without obvious signs of rheumatic or other infective heart disease, should be the occasion for a thorough examination of the patient for signs of exophthalmic goitre.

The Senile Heart.—This clinical group is due to the effects of arteriosclerosis and to the lesion known to morbid anatomists as fatty infiltration. The former produces thickening and calcification of valves and various lesions in the coronary arteries, embolism, thrombosis and ischemic necrosis. The clinical types include sudden cardiac failure, especially under the stress of hot weather, overexertion or an anesthetic, aortic stenosis, general cardiac failure, angina pectoris and acute abdominal pain simulating inflammation of the gall-bladder or perforated gastric ulcer.

Morbid Anatomy and Histology.—Pathological anatomy can seldom answer the question whether a heart is insufficient to carry on its work. Many hearts that have not adequately performed their work during life hardly differ from normal hearts. But although we have not learned to recognize all the conditions in the heart which give rise to cardiac failure, the anatomical effects in other organs are very striking—the cardiac liver and spleen afford a sure means of determining death from heart failure. The reserve power of the heart in a large number of persons is very small, and therefore a very insignificant lesion might produce a great upset in the circulatory balance if the recuperative power were small. Again, conditions of nutrition exercise a marked effect, for instance, old age, anemia, and tuberculosis may give rise to lesions recognizable with difficulty.

The hypertrophied heart is not as good as a normal heart. This is a clinical fact about which there can be no two opinions, and by a hypertrophied heart we mean one which gives definite signs of enlargement

and therefore probably dilatation. Martius endeavored to explain this by saying that a definite amount of reserve power is at the disposal of the heart, and if more of this is used for ordinary purposes the less there will be for purposes beyond the ordinary. As it stands this can hardly be strictly true, for Hasenfeld and Romberg¹ showed that a heart hypertrophied as the result of an artificial valvular lesion has practically the same reserve power as a normal heart. This, however, is not the case in valvular lesions in man, especially when there is some considerable hypertrophy, and it must then be supposed either that the limits of the normal working energy expended at rest are much overstepped or that in addition to the valvular defect there are others in the myocardium. In the commonest cause of valvular deficiency, namely, rheumatic fever, this is now certain. Aschoff and Tawara have described, in the muscle of such hearts, accumulations of large cells and giant cells, miliary and sub-miliary in size, in the connective tissue separating the muscle fibres, or in the subendocardial tissue; these collections have been seen partly or wholly destroying the branches of the conducting system of fibres (Purkinje's fibres).

Much has been done in the way of a systematic search after the anatomical changes which underlie heart failure. The pioneers in this work have been Krehl and Romberg and their pupils of the Leipsic school. It cannot yet be said that there is any unanimity in the opinions. The cases from which these results have been obtained are those dying from various forms of heart failure, especially valvular lesions, chronic hypertrophy from overindulgence in alcohol or renal disease. Changes have been described in the nuclei, in the amount of pigment and fat, but neither these nor fragmentation of fibres, round-cell accumulations, or areas of fibrous tissue seem sufficient to throw any light on the problem.

Lesions of Special Muscle Bundles.—Albrecht, following the idea that heart insufficiency was due to lesions of particular bundles of muscle fibres, has attempted to show, on the basis of anatomical preparations, chiefly from the sheep's heart, that particular bundles of muscle fibres are affected, especially in the left ventricle, one connecting the posterior part of the ventricular septum with the posterior papillary muscle. Albrecht's conclusions have not been confirmed.

The Conducting System of Muscle Fibres.—A lesion of the bundle of His may give rise to the group of symptoms known as Stokes-Adams disease. Tawara demonstrated that this bundle began in the neighborhood of the coronary sinus, in muscle fibres which were easily distinguishable from those of the auricular muscle itself. Shortly before entering the fibrous body of the heart the fibres interlace with one another, and here Tawara gives it the name of Knoten. It then pierces the fibrous body of the heart and appears on the top of the muscular septum of the ventricles, where it divides into right and left branches. These branches are subendocardial, the left spreading out into a fan-shaped area on the septal wall of the left ventricle, the right descending in a chink between two muscle columns on the septal wall of the right ventricle, giving off small

¹ *Arch. f. exp. Path.*, Leipsic, 1897, **39**, 333.

branches to the neighboring muscle on its course. The ultimate ramifications of the bundle consists of Purkinje fibres, and are found on the surface of the muscle columns and as the false chordæ tendineæ, the whole being a system partly to convey muscular impulses from the auricle to the various parts of the ventricle, and partly in all probability to allow for a re-inception of the rhythm if the normal source should fail; the Purkinje fibres, being more primitive in structure, apparently retain in greater completeness their primitive functions, especially that of rhythmicity.

The right and left limbs of the bundle both convey fibres to the papillary muscles, the median papillary muscle of the right ventricle being supplied by a recurrent branch from the right limb.

Later Keith and Flack demonstrated that this system of fibres is of even greater significance. They have shown that in mammals, especially the mole, and in man there is a system of fibres at the origin of the great veins whose structure is easily distinguishable both from that of the venous muscle and that of the neighboring heart muscle. This muscular tissue is extremely like that in Tawara's system, and can be traced into the "Knoten" before named as well as in other directions. The muscular tissue at the roots of the veins sends branches to both auricles and the interauricular septum.

We have in this system, therefore, a complete skeleton of undifferentiated muscular tissue, added to which are the more differentiated parts of the heart. It serves the purpose of originating the impulse at the origin of the great veins and of conveying muscular impulses to the various parts of the heart. Aschoff and Tawara emphasize the importance of taking into account this system and its lesions in cases of heart failure. Albrecht certainly had the right notion in his attempt to find lesions of particular bundles of muscle tissue when explaining heart failure. Aschoff and Tawara have shown that in heart failure in acute rheumatic fever many of the lesions invade more especially the sites of the branches of this system. A thorough re-investigation of the subject of the anatomical changes in heart failure based on the knowledge of this system is much to be desired.

Symptoms of Chronic Cardiac Failure.—(a) *Alimentary System.*—The most important are loss of appetite, indigestion, feelings of distention, vomiting, pain in the abdomen, flatulence, meteorism, constipation, and hemorrhoids.

Two causes participate in producing these disturbances: First, the relations of the heart and stomach are such that any increase in the size of the stomach would interfere with the contractions of the heart, and at the same time even a moderate distention would interfere with the movements of the diaphragm; second, any failure of the right side of the heart produces an overfilling of the bloodvessels, slowing of the circulation, and consequent impairment of the organs of the abdomen. The actual condition of the organs in the latter state is one of venous congestion, with or without œdema, catarrhal processes are present on all free surfaces—stomach, intestines, bile ducts, etc. Loss of appetite and indigestion are frequent signs of heart failure. They may be the first things brought to

the patient's notice, and in the later stages, especially those in which the right side of the heart is at fault, they may be distressing, the patient preferring to be without food rather than submit himself to the discomfort attendant upon eating. With the inability of the stomach properly to digest or forward its contents the food undergoes fermentation with the production of gas; when this assumes a certain magnitude the distention impedes both respiration and cardiac action, and distress follows. Relief almost invariably follows copious eructations of the accumulated gas, but this not infrequently is difficult to attain, owing to deficient muscular power in the stomach itself and in the abdominal muscles.

Vomiting is not particularly common except under two conditions: it is met with frequently as a sign of heart failure in athletes after a hard race, and, secondly, it is a constant accompaniment of the later stages of any chronic form of heart failure; in the latter it is often a very bad prognostic sign. It is not possible at present to describe the mechanism by which this symptom arises; it seems to be an effect rather of left-sided than of right-sided heart failure, consequently we might attribute it to a deficiency in the blood supply to the medulla and a stimulation of the vomiting centre. This would receive some support from the analogy of the vomiting that occurs in shock. We must not lose sight, however, of the possibility of its also being due to a reflex stimulation of the vomiting centre by means of afferent impulses transmitted up the vagus fibres from the heart or stomach.

Pain in the abdomen may be dull and aching or sharp and lancinating. It may have its origin in the stomach from the condition set up there; it may be due to the distention of the liver and stretching of its capsule; a tender liver in heart disease is of frequent occurrence and may be a very early sign of chronic heart failure. On the other hand, it may be due to conditions in the intestine. It may be caused by an infarct in one of the mesenteric arteries. And last, it may be caused from angina, the pain being referred to the abdomen.

Any accumulation of gas in the intestine adds to the distress of the patient from the same reason as distention of the stomach; hence the necessity of special attention to the bowels. With the diminution in secretory activity there comes also a diminution in motility and constipation, which is often troublesome. On the other hand, the œdema may be great and the irritation increased to such an extent that diarrhœa is produced. Any condition of back pressure in the portal system acts unfavorably on those places where the portal and systemic system communicate; hemorrhoids, therefore, are frequent.

(b) *Cardiovascular System*.—Symptoms connected with this—the system that is at fault—are remarkably few. Palpitation is sometimes complained of, especially in those with large hearts. The patient is sometimes aware of a feeling of fulness in the chest, but this again may proceed from the abdominal organs. Pain referred actually to the cardiac region is infrequent; it is usual, of course, in inflammatory conditions of the pericardium, but here it is due undoubtedly to the stimulation of the nerves of the pericardium and not to any heart failure as such. Pain which is referred to other parts of the body, such as in the neck, down the arms, etc., is almost invariably anginoid.

(c) *Respiratory System.*—Under this heading come hyperpnœa, orthopnœa, and dyspnœa, attacks of dyspnœa—the so-called cardiac asthma—Cheyne-Stokes respiration, cough, hæmatemesis, and pain.

The various forms of dyspnœa seem usually connected with failure of the right side of the heart and are accompanied by some cyanosis. The rate and depth of breathing are regulated by the amount of carbon dioxide which reaches the respiratory centre in a given time, or, in other words, if the tension of carbon dioxide in the blood remains the same, the circulation being unaltered, the rate and depth of respiration will not vary. If by an increase of the percentage of carbon dioxide in the air breathed in less is able to diffuse out from the blood, there is an immediate change in the amplitude of respiration which corresponds accurately with the tension of carbon dioxide in the alveolar air. The tension of CO_2 in alveolar air rises during exercise owing to an increased amount being set free; consequently an increased ventilation takes place. From these experiments it is natural to conclude that hyperpnœa and dyspnœa are such common features in heart failure because of a deficient elimination of carbon dioxide by the lungs, due primarily to a deficiency in the heart and a slowing of the circulation in the lungs.

It is well to limit the term *hyperpnœa* to an increase in the rate and depth of respirations, applying the term *dyspnœa* only to conditions in which there is distinct distress. *Orthopnœa* is that condition of hyperpnœa in which the patient assumes the upright position of the trunk, any attempt to lie down being immediately followed by an increase in respiratory distress. Its origin has been attributed to the mechanical conditions in the abdomen and neighborhood of the diaphragm. When orthopnœa is present the abdominal organs supplied by the portal vein are distended partly by blood and partly by œdema fluid. The hyperpnœa necessitates the greatest possible movement of the diaphragm and, if the contents of the abdomen are followed in a small degree to press against it, the force required in order to effect the necessary ventilation of the lungs must be greater.

Another factor must be taken into account in considering dyspnœa in cardiac disease. V. Basch supposes that, other things being the same, the extensibility of the lungs becomes less in proportion as the pressure of the blood in the capillaries of the lungs becomes greater, that with greater filling of the lung capillaries the lungs become stiffer. This condition he calls "*Lungenstarrheit*." It hinders both the expansion of the lungs on inspiration and their contraction on expiration. With the same overfilling of the lungs with blood, owing to a straightening out of the capillaries in the walls of the alveoli, there is an enlargement of the cavity of the alveolus which gives rise to an enlargement of the whole lung (*Lungenschwellung*). Both of these conditions would act so as to require a greater expenditure of muscular force to effect the normal ventilation of the lungs. Although the general truth of the proposition is admitted and has been demonstrated by experiment, there is as yet not evidence enough to assert that under the conditions of congestion of the lungs occurring in heart disease it is present to a degree capable of offering a great hindrance to respiration. Though the dramatic effects of bleeding might be thought to confirm the hypothesis.

In the sudden attacks of dyspnoea known as "cardiac asthma" we must look probably to other causes than those just mentioned. The attacks usually come on at night at the same time as some of the paroxysmal neuroses. The onset is sudden, the distress great, the face is usually pale and cyanosis is absent. The pulse is rapid, soft, and irregular in force and frequency and the attacks frequently coincide with cardiac signs such as gallop rhythm or pulsus alternans (Lewis). There is an overloading of the right heart and insufficiency of the left. Recent work suggests that the rate of flow in the systemic veins is increased. The alkalinity of the blood is increased. François-Franck found that irritation of the heart or aorta produced reflex respiratory phenomena, such as spasm of the larynx and bronchi, which was intensified by the coexistence of a valvular lesion. "Cardiac asthma" may be the first sign of heart failure to the patient; it may come on after excitement, a meal, the slightest extra exertion, or without any adequate reason. Krehl notes the frequency of "cardiac asthma" in arteriosclerosis, coronary artery disease, and nephritis, and from the features of the attack and the association with cardiac disease supposes that it is due to temporary weakness of the left ventricle and some increase of pressure and loss of velocity of the blood in the lungs.

Cough in cardiac disease occurs first in acute cardiac failure under the same conditions as vomiting in overexertion: in fact, coughing is frequently suggestive of a milder form of cardiac failure, vomiting appearing later and in the severer forms. It may occur in chronic cases probably from failure of the medullary circulation. But by far the most common cause of its appearance is the reflex stimulation of afferent nerves to the respiratory centre in the medulla. Changes in the pleura and accumulation of fluid may produce the same.

Hemoptysis is very common in cardiac failure, especially in mitral stenosis. It may vary from a sudden profuse hemorrhage to slight streaks of blood in the sputum. When it occurs early in the course of a mitral stenosis it may be looked upon as compensatory and a relief to an overfilled lesser circulation. In the later stages of mitral failure small hemorrhages are frequent. From postmortem records we know that in these cases there is often marked sclerosis of the pulmonary vessels; many of these probably have weakened spots and, with the continuance of the increased pressure, give way, causing hemorrhage into the lungs and bronchi, but the more frequent origin of hemoptysis is infarction of the lungs following an embolus detached from the right auricular appendix. If such an embolus be small the hemorrhage is minimal and no consolidation of the lung can be found even though there be pain on the affected side. Larger emboli give rise to greater hemorrhage of the "prune juice" variety with a patch of bronchial breathing toward the edge of the lung with perhaps later a pleuritic rub.

(d) *Central Nervous System*.—Apart from the symptoms due to gross brain disease, such as embolism, thrombosis, hemorrhage, etc., there are many symptoms whose origin is not clear.

Increase of brain activity, sleeplessness, and mania are not infrequent. Two factors must be thought of: first, lack of nourishment from insuffi-

cient filling of capillaries, and, secondly, uremia. Of uremia in cardiac disease we know little; it may come on from continual disturbance of the kidney cells from insufficient arterial blood supply, from pressure on the kidneys due to ascites, and possibly from other conditions.

Unconsciousness in heart disease comes on when there is a marked deficiency in the amount of blood that reaches the brain, and in those in whom the deficiency remains death results. It is not always possible to attribute fainting attacks in normal persons to momentary deficiency in heart action; many such may be due to sudden loss of tonus in the splanchnic area, but since we know that a sudden stoppage of the heart can be produced by the action of the vagus nerve it is right to assume that some attacks of fainting are due to lack of proper blood supply to the brain. The same objection cannot hold when the heart itself is at fault. Sudden fainting in fatty degeneration of the heart and in coronary artery disease with a fatal termination is well known. One of the common symptoms of aortic disease, often that which first comes to the notice of the patient, is fainting. In aortic disease, if a proper supply of blood is to be given to the brain, the minimum blood pressure must be kept above a certain limit. The blood pressure in aortic disease varies between very wide limits; the maximum is frequently great, 150 to 160 mm., and the minimum may be any figure below 80 mm. To prevent lack of cerebral blood it is necessary that this minimum should not be unduly lowered. But if the pulse intermits or has an extrasystole and a longer interval between two normal beats, the outflow from the aorta into the heart is not adequately checked during the period of the abortive beat and the system becomes abnormally empty.

Stupor and drowsiness are seldom seen except toward the end of life or in very severe cardiac disturbance. Probably the same cause acts here as in unconsciousness, the failure of the left ventricle properly to fill the arterial system; but from its presence in cases in which the right side of the heart is mainly at fault, with great cyanosis and œdema, we must take into account the possibility of its being due to a chronic poisoning by carbon dioxide with which the capillary blood is overcharged.

Epileptiform Convulsions.—The attention given to the study of Stokes-Adams disease leaves no doubt that cerebral anemia can give rise to unconsciousness, and also to convulsions. In Stokes-Adams disease there are differences in the onset of the convulsions, but usually, as in the patient described by Webster,¹ in whom the heart would intermit for periods of ten to twenty seconds, the first warning was pallor of the face coincident with a disappearance of the pulse at the wrist; after some fifteen seconds of absence of the pulse, spasmodic twitchings of the muscles of the face were observed; as the period increased the spasmodic movements spread first to the muscles of the neck and ultimately to the arms, trunk, and leg. With the more severe attacks there was concomitant squint or conjugate deviation of both eyes to one or other side. The pupils were widely dilated, respiration was noisy, and froth appeared at the mouth. Unconsciousness during the greater part of the period was complete, and with

¹ *Glasgow Hospital Reports*, 1900, 3, 413.

the return of consciousness flushing of the face occurred with the appearance of the pulse at the wrist. The classical experiments on this aspect of the circulation were made by Kussmaul and Tenner.¹

(e) *Integumentary System*.—Cyanosis is due to an overabundance of reduced hemoglobin in the vessels of the skin. It is not necessarily associated with heart disease. Many normal persons continually have blue hands, ears, and cheeks; in these cases local conditions of the circulation are the cause, for it seldom affects the lips. The blood from cyanosed areas shows polycythemia. Petechial hemorrhages or focal necroses are seen in the malignant varieties of endocarditis. Senile gangrene occurs in ischemic necrosis of the cardiac muscle.

Œdema.—The œdema of cardiac disease occurs first in those parts of the body which are most dependent, in the ankles if the patient is out of bed, in the buttocks or calves if the patient is in bed. The skin looks thin and more transparent; if the œdema is great it may be smooth and shiny. Most patients complain of some pain on pressure over œdematous parts. If the œdema has lasted for a month or two or if the patient has been walking about, the œdema becomes very hard.

Richard Lower, in 1680, first showed the connection of increased pressure in the veins with the production of œdema; he found that œdema of both lower limbs came on as the result of tying the inferior vena cava; on this experiment he explained the presence of œdema in cardiac disease. There are three possibilities for an explanation of cardiac œdema whose immediate cause is an overfilling of the veins; it may be due to an increase of pressure and filtration of œdema fluid from the vessels from which transudation normally takes place, namely, in the capillaries; it may be due to an alteration in the permeability of the vessel wall, or it may be due to an increased secretory activity on the part of the cells of the capillary walls. Increase of pressure in the capillaries, although it undoubtedly occurs in cardiac disease, is not the immediate factor in its production, for cutting the vasomotor nerves to a limb and stimulating the spinal cord to produce a dilatation of the small arteries and an increase in aortic blood-pressure respectively does not result in any œdema of the limb. Again, if the pressure was the immediate cause of the exudation, tying of the veins should in a short time be followed by an increased lymph flow and the appearance of œdema, but these only appear several hours after the increase of pressure.

The factor of importance is the lack of proper nutrition, both liquid and gaseous, to the tissues as well as an interference with the removal of waste products. If hemostasis is produced in a limb for an hour, by tying a ligature tightly around it, the specific gravity of the venous blood and of the plasma rises and the lymph flow falls; after the removal of the ligature a small increase of venous pressure easily gives rise to œdema. The tendency to œdema is great if the limb has been rendered anemic for an hour by means of an Esmarch bandage. These experiments show the importance of the tissues in the formation of cardiac œdema as opposed to the view first enunciated by Ludwig, that it is due exclusively

¹ Kussmaul and Tenner, *The Nature and Origin of Epileptiform Convulsions Caused by Profuse Bleeding*, *New Sydenham Society*, London, 1859, translated by Edward Bonner.

to the conditions of pressure in the capillaries. Whether the œdema of cardiac disease is a filtrate or a secretion cannot yet be decided.

(f) *Renal Conditions in Cardiac Disease.*—The features of the urine in cardiac insufficiency of a high grade are as follows: A great lessening in the total amount excreted, even to a half or less than the amount excreted before on the same intake of fluid; the color becomes darker, with that the concentration is greater and the specific gravity rises; the reaction is usually strongly acid; deposits after standing are very common. The urea reaches about 5 per cent. in the concentrated urine. The uric acid is often in relatively greater amount than under normal circumstances. Leucin and tyrosin can be found in the urine of patients in whom the liver is enlarged from cardiac disease. The inorganic salts vary considerably in amount. A small amount of albumin is usually found. The sediment contains in a large number of cases white-blood cells, an occasional red cell, and a few casts, most frequently hyaline, but sometimes granular and even cellular ones are found.

These changes are found only in those cases in which the function of the right side of the heart is at fault, accompanied by congestion in the venous system. To do its work properly the kidney must be supplied with its normal amount of arterial blood, for if not, the cells form large quantities of sarcolactic acid and undergo changes which are the beginnings of necrosis. The large amount of sarcolactic acid will account for the constant and well-marked acidity of the urine in cardiac patients; the necrotic changes in the cells of the tubules will account for the increase of uric acid and the presence of albumin; it is not so easy to account for the concentration of the urine. It might have been thought that as the kidney partakes in the tendency to become œdematous the urine would have been more diluted, but normally the concentration of the urine seems to be determined on the one hand by conditions of the blood and on the other hand by the conditions of the blood supply. If the sweat glands are excreting vigorously, the urine contains less water and rises in specific gravity. If, on the other hand, the peripheral arteries are constricted and the blood-pressure rises in the internal organs of the body, the kidneys, as under the influence of cold, excrete a large amount of dilute urine. We must probably look to the constant loss of the watery constituents of the blood in the form of œdema fluid elsewhere as the reason for the high specific gravity of the urine, for the blood in conditions with œdema is more concentrated. Further, the formation of œdema fluid takes place as a transudate from the veins rather than from the capillaries nearest the arteries which are more concerned in the secretion of urine.

The Blood-pressure in Relation to Cardiac Failure.—It was hoped that some indication of the state of the heart was to be found in the records of blood-pressure. Such a hope has hardly been justified. In most of the published records of blood-pressure the maximum is the only one recorded, but when one considers that in a case of irregular heart from mitral failure the summits of the pulse waves on a tracing vary considerably it is obvious that no constant value can be obtained.

It is different, however, if we take the maximum record obtainable.

If one is dealing with young adults without evidence of renal disease an estimate of their maximum blood-pressure at something less than 125 mm. of mercury is probably within the limits apart from psychical or other disturbances. In early heart failure, such as can be seen in anemic girls, the blood-pressure is higher than is expected and may be high when the pulse at the wrist is small and feeble. It may be an evidence of a compensatory mechanism, probably a peripheral arterial constriction directed toward an adequate upkeep of average blood-pressure. It has been found that cardiac patients on improvement of the circulation in the majority show a fall of blood-pressure and that the pulse-pressure becomes less. The blood-pressure in cardiac disease bears no relation to the degree of dyspnœa or œdema.

The difficulty of determining by clinical methods the extent to which any given heart can do extra work is a serious deficiency in the matter of forming an opinion for the future guidance of the patient. Some hearts, for instance, although hypertrophied, will show no signs of failure for many years; others, again, even though the hypertrophy may only be small and not of long duration, may often show signs of heart failure, sometimes acute in its onset.

Treatment.—This is discussed in the section on Valvular Diseases.

CHAPTER XIX

DISEASES OF THE VALVES OF THE HEART

BY THE LATE SIR WILLIAM OSLER, BART., M.D., F.R.S.,

AND

ALEXANDER G. GIBSON, M.D., F.R.C.P.

INTRODUCTION.

General Etiology and Morbid Anatomy.—Acquired valvular defects are the sequence of acute endocarditis or the result of a primary fibrosis. In both cases the effect is the same—a deformity, puckering, and adhesion of the valves, leading to insufficiency or stenosis, or to both combined. Chronic disease of the valves of the heart, then, is a question almost exclusively of valvular fibrosis.

In about 50 per cent. of all the cases this sclerosis is a sequence of acute endocarditis. Among 670 cases of chronic heart disease at the Leipsic clinic, 58.5 per cent. followed acute rheumatism (Romberg). Other acute diseases of childhood are responsible for a certain number of cases, while in a not inconsiderable proportion, particularly of mitral cases, no etiological factor can be determined. Syphilis, especially of the aortic valves is an important factor. There is a senile arteriosclerotic form which follows the ordinary wear and tear of life. All conditions which keep up permanent high tension lead to some thickening of the aortic and mitral segments; while certain poisons, alcohol and tobacco, may cause primary sclerotic changes in the valves, just as they do in the arteries. The morbid anatomy of chronic rheumatic valvular fibrosis is very characteristic. In the early stages the edges of the valves are a little thickened and may present nodular bodies, the remnants of organized vegetations. In the aortic segments the corpora Arantii enlarge, the edges thicken, the substance of the valve loses its translucency, and along the line of attachment to the aorta there is opaque sclerosis. In the auriculo-ventricular valves these early changes are seen just within the margin, and here it is not uncommon to find swellings of a grayish-red, somewhat infiltrated appearance, almost identical with the similar structures on the intima of the aorta in arteriosclerosis. Even early there may be seen yellow or opaque white subintimal fatty degenerated areas. As the sclerotic changes increase, the fibrous tissue contracts and produces thickening and deformity of the segment, the edges of which become round, curled, and incapable of that delicate apposition necessary for perfect closure. A sigmoid valve may be narrowed one-fourth or even one-third across its face, the most extreme grade of insufficiency being induced without any special deformity and without any narrowing of the

arterial orifice. In the auriculo-ventricular segments a simple process of thickening and curling of the edges of the valves, inducing a failure to close without forming any obstruction to the normal course of the blood flow, is less common. Still, we meet with instances at the mitral orifice, particularly in children, in which the edges of the valves are curled and thickened, so that there is extreme insufficiency without any material narrowing of the orifice. More frequently, as the disease advances, the chordæ tendinæ become thickened, first at the valvular ends and then along their course. The edges of the valves at their angles are gradually drawn together and there is a narrowing of the orifice, leading in the aorta to more or less stenosis, and in the left auriculo-ventricular orifice—the two sites most frequently involved—to constriction. In arteriosclerotic thickening there is less puckering and contraction. The aortic leaflets show thickening and sometimes coalesce and always if the process advances become more rigid. The mitral valve shows a thickening of all its parts with perhaps an atheromatous plaque in the anterior leaflet but there is no retraction or thickening of the chordæ tendinæ.

Finally, in the sclerotic and necrotic tissues, lime salts are deposited and may even reach the deeper structures of the fibrous rings, so that the entire valve becomes a dense calcareous mass with scarcely a remnant of normal tissue. The chordæ tendinæ in rheumatic cases may gradually become shortened, greatly thickened, and in extreme cases the papillary muscles are implanted directly upon the sclerotic and deformed valve. The apices of the papillary muscles usually show marked fibroid change.

Incidence of Involvement of the Valves.—In the collected statistics of Parrot the mitral orifice was involved in 621 cases, the aortic in 380, the tricuspid in 46, and the pulmonary in 11.

Mortality.—The average number of deaths per year in England and Wales from disease of the circulatory system during the decade ending in 1913 was 82510.7; for the decade ending in 1923 the total average was 68448.5. The death rate per 1000 from circulatory disease in the similar periods is 1.93 and 1.79 respectively. When one considers that a very large proportion of these cases have their origin in rheumatic fever, we see what an important role this disease plays among the acute infections. Whether we take circulatory disease, cardiac diseases or rheumatic fever, there is a slightly greater proportion of females over males.

Age Incidence.—Fully one-half of the cases of valvular disease of the heart occur in young persons. Up to the fifth year children are not very liable to valvular disease, but from the fifth to the tenth a great many cases of chorea and rheumatic fever lay the foundation for subsequent sclerotic changes. Doubtless, many cases of mitral disease owe their origin to the slight valvulitis arising in the course of a tonsillitis. Between the tenth and fifteenth years there is an ever-increasing liability. From this time, onward, the endocarditic valve lesions diminish. During the adult period, from the twentieth to the thirtieth year, the maximum number of cases of cardiac breakdown occur—37.16 per cent. in Romberg's Leipsic statistics. In the fourth decade a considerable number of the endocarditis cases drop out and the special sclerotic forms begin to appear, more particularly the syphilitic and those associated with the toxic types

of sclerosis. Through the fifth, sixth, and seventh decades there is a progressively diminishing incidence. The figures in Romberg's statistics were for the fifth decade, 12.69 per cent.; for the sixth, 9.10 per cent.; for the seventh, 4.33 per cent.; and for the eighth, 1.05 per cent.

Effects of the Valve Lesions.—The general influence on the work of the heart may be briefly stated as follows: The sclerosis induces insufficiency or stenosis, separately or in combination. Narrowing retards the normal outflow; insufficiency permits a certain reflux of blood, with the effect of dilatation of the chamber behind the affected valve. In the former case the chamber has a difficulty in expelling its contents through the narrow orifice; in the latter the chamber is overfilled by blood flowing into it from an improper source, as, for instance, in mitral insufficiency, when the left auricle receives a double current from the pulmonary veins and from the left ventricle.

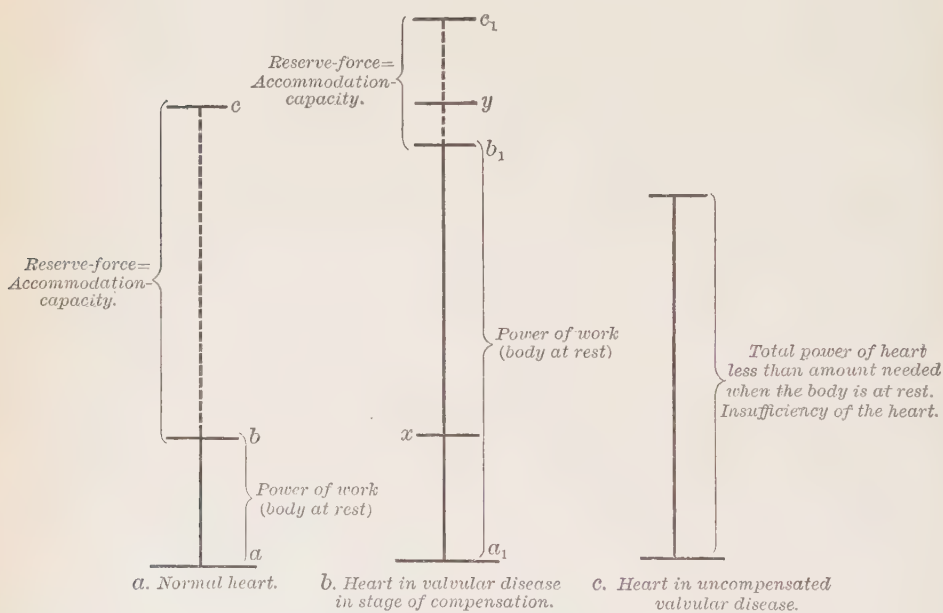
The heart is fully prepared to meet the ordinary grades of dilatation which constantly arise during the extra calls of exertion, when, as in the course of a fever, its muscle has been enfeebled. Supposing as in valvular disease, the dilatation of a cavity is permanent, then the constant extra stimulation of the heart required to keep the circulation properly maintained calls forth hypertrophy (see article on Hypertrophy) to combat this extra constant demand upon the heart's resources. When the inception of valvular disease is slow, as from sclerotic changes, the increased activity of heart muscle calling forth a gradual hypertrophy is able to avert any lack of compensation until the valvular deficiency oversteps the limits which increased activity and hypertrophy can oppose. On the other hand, if the valvular defect occurs rapidly, then compensation is disturbed in proportion to the magnitude of the deficiency and its rate of onset, and the heart remains uncompensated until hypertrophy has time to develop. To appreciate its nature the process may be graphically shown in the accompanying diagrams, in which the perpendicular lines represent the power of the work of the heart. While the muscle in the healthy heart (Fig. 36 *a*) has at its disposal the maximal force, $a\ c$, it carries on its work under ordinary circumstances (when the body is at rest) with the force $a\ b$; and $b\ c$ is the reserve by means of which the heart accommodates itself to greater exertion.

With a gross valvular lesion the force needed to do the ordinary work (at rest) becomes very much increased (Fig. 36 *b*). But in spite of this enormous call for force, insufficiency of the heart muscle does not necessarily result, for the working force required is still within the limits of the maximal power of the heart, $a_1\ b_1$ being less than $a_1\ c_1$. The muscle accommodates itself to the new conditions by making its reserve mobile. But this condition could not be permanently maintained, for there is nothing left for emergencies but the small reserve force $b_1\ y$. Even when at rest, the heart would be using continuously almost its maximal power. Any slight exertion requiring more extra force than that represented by the small value $b_1\ y$ (say the effort required in walking or in going up stairs) would bring the heart to the limit of its working power and palpitation and dyspnoea would appear. The increased exertion leads now to the putting on of yet more muscle, enabling the heart the better to meet

the added calls on its strength, and with this the extreme limit of cardiac action is raised, and instead of this being at y , it now reaches c_1 , provided there is no interference with the nutrition of the heart muscle.

To what extent the various degrees of valvular insufficiency call forth an increase in reserve power is difficult to decide. It is probable that with a slight lesion the limit at first is not beyond what it would be in a similar normal heart under the same conditions, but when the requirements of the heart, with the body at rest, increase so as to approach the limit of the reserve power, we may infer that the total cardiac capacity is increased in proportion because, unless absolute rest of the body, and probably also of mind, is maintained, any movement and any excitement increase the work of the heart and widen the upper limit of cardiac capacity.

FIG. 36



(After Martius.)

The property of the heart whereby at times greater work can be sustained than when the organ is at rest has an important bearing on the course and the treatment of organic lesions. *Per se*, a valvular lesion if slight may affect but little, if at all, the limits to which cardiac action can be pushed; in other words, a person with a well-marked valvular lesion sometimes undergoes, without any outward symptoms of excessive distress, the most arduous trials of endurance. But it must not be supposed that a person with valvular disease can undergo with impunity as arduous, continuous exercise as a person with a normal heart. Because, first, the total work required of such a heart at the height of the exertion is far above that asked of the normal heart under similar circumstances;

secondly, valvular lesions in man, especially of rheumatic origin, hardly ever leave the muscle in the same state as before, so that less work can be got out of it and the inevitable dilatation leads to a yet further increase in the heart's requirements at rest.

The Reserve, a function of cardiac muscle alone, is well marked in youth and increased up to adult age and thereafter diminishes; it is also affected by any interference with cardiac muscle, such as infections, intoxications, malnutrition. In all valvular lesions these rest and reserve capacities should receive consideration. In the early periods, the heart's work should be well within the rest limit, so as to throw as little strain as possible on the affected valves and allow healing to take place. When this is accomplished, exercise should be so regulated that the reserve is not called upon too suddenly or too freely, while at the same time the limits of cardiac response are gradually widened. If we condemn a person with valvular disease to live always at or about his rest limits, we may tend to retard the growth of his cardiac reserve. On the other hand, it would invite an attack of cardiac failure to ask him to do an arduous piece of work, or if he had to undergo a serious infection. In valvular disease, although an increased amount of work is demanded of the heart, with the body at rest, the full reserve should, if possible—the part *b* to *c* in the diagram—be developed and maintained in young persons, in whom normally these limits are easily extended by daily exercise. There is no reason why a lad with valvular disease should not in a modified degree undergo the same training as a healthy one. In persons who have arrived at an age when cardiac muscle begins to degenerate, the greatest care must be taken. In compensated lesions, exercise of the heart, *i. e.*, work over and above the rest limit, is usually beneficial, but a thorough survey of the patient's cardiac condition should be made from time to time, and the effects of this exercise carefully studied. A heart which undergoes increased exertion gets a hypertrophy of work, enlarging in all its parts and increasing in weight. But although the cavities enlarge somewhat, they do so probably in some (as yet unknown) proportion to the increase in the bulk of the muscle. On the other hand, hypertrophy that follows a valvular deficiency results from the enlargement of a cavity beyond the normal limits to allow of accommodation. Without such hypertrophy the circulation would not be adequately maintained even at rest. The hypertrophy of valvular disease is to be compared accurately with that from overexertion, due in both to a dilatation of one or more cardiac cavities. If a valvular deficiency could be made good, we should expect a return of the organ to normal bulk, for no other reason than that the cavity has again resumed its normal, or nearly its normal, size at the beginning of systole.

No doubt the capacity of the heart to hypertrophy in valvular disease is limited by the extent to which the hypertrophy of work can be attained, and such a result in an aged person is not so easily compensated as in a younger one, and the greater the insufficiency the less chance there is to increase the limits of cardiac reserve by hypertrophy.

Turning now to the disturbance of *compensation*, it is to be borne in mind that any heart, normal or diseased, may become insufficient when—

ever the call for work exceeds the maximal capacity. The liability to such disturbance will depend, above all, upon the accommodation limits of the heart, the less the width of the latter, the easier will it be to go beyond the heart's efficiency. A comparison of diagrams *a* and *b* (Fig. 36) will immediately make it clear that the heart in valvular disease will become insufficient much earlier than the heart of a healthy person. If the heart muscle be compelled to do maximal or nearly maximal work for a long time it becomes exhausted; or, to be more specific, the mechanism by which extra work is called forth from the heart, namely, stimulation of the heart muscle by stretching, and reflexly by the sympathetic nerves from underfilling of the peripheral vessels, fails to act further; the muscle now becomes more stretched, the blood supply is interfered with, and the circulation becomes insufficient at that point. In valvular disease, on account of its small amount of reserve force, the heart has to do maximal or nearly maximal work far more frequently than does the normal heart. By stretching of its walls or interference from myocardial degeneration or disease, its power falls below the amount necessary to carry on the work of the heart when the body is at rest, or it may cease to be sufficient even for this. The reserve force gained through the compensatory process may be entirely lost (Fig. 36 *c*). On the other hand, the insufficiency of the valve at fault may make demands on the heart up to such a point that it approaches and oversteps the upper limit of cardiac accommodation. In the first case, if the loss of reserve force is only temporary, *i. e.*, if the demands on the heart are lessened by rest, or if the muscle can be allowed to recover, the condition is spoken of as a "disturbance of compensation." The term decompensation or "loss of compensation" is reserved for the condition in which the disturbance is permanent.

INSUFFICIENCY OF THE AORTIC VALVES.

Etiology and Morbid Anatomy.—The aortic valves become insufficient under many different conditions, which are important to recognize, particularly as they have a bearing on prognosis.

The frequency of the disease varies in different localities and in different hospitals. Where the patients are from the working classes in large manufacturing centres, and in seaport towns where syphilis prevails, the number of cases is very large. On the other hand, in hospitals with a large proportion of children, aortic insufficiency is relatively rare.

One of the most carefully compiled sets of figures is that from the Edinburgh Infirmary.¹ Of 2368 cases with cardiac lesions, valvular disease occurred in 80.8 per cent. (1914 cases); 7.3 per cent. of these 1914 cases were aortic insufficiency alone and 17.6 per cent. aortic insufficiency with mitral disease. Barié gives the proportion at 37 per cent. It is the most common form of aortic valvular disease and occurs much more often than stenosis. The ratio between stenosis and insufficiency is very variously given, owing to the fact that the recognition of

¹ Gillespie, *Edinburgh Hospital Reports*, 1898, 5, 31.

the former is not nearly so easy, as in many instances the diagnosis of stenosis has rested simply on the presence of a basic systolic murmur.

Age.—It is comparatively rare in childhood, and is most common in men in the fifth and sixth decades. The form following endocarditis occurs at an earlier age, and is met with in children and young adults. The luetic form is met with in comparatively young men. The arterio-sclerotic form occurs after the age of sixty.

The cases may be divided according to their mode of origin.

1. **Endocarditic.**—The acute infections with which endocarditis is associated, attack the aortic and mitral valves with varying frequency. Rheumatic fever and chorea have a special predilection for the mitral segments. The ordinary septic types attack aortic and mitral valves alike. The severe pneumococcic and gonococcic forms are perhaps seen more frequently on the aortic segments. The ordinary endocarditis of rheumatic fever in children, even when it attacks the aortic valves, may not leave them incompetent. The chaplets of little vegetations may disappear without leaving much, if any, damage. In other cases the edge of one or of two valves is thickened, slightly curled, so that they do not come into close apposition during diastole, and in consequence there is a slight leak. In yet a third group of cases endocarditis has been more severe. The substance of the valve itself has been involved. The segments become adherent, calcification takes place in the hyaline and necrotic tissue, so that the aortic orifice is itself narrowed and there is a combination of stenosis and insufficiency. Sometimes, as a result of the endocarditis, one valve only is affected and a rigid calcified spur remains which prevents the proper closure of the valve. The distinguishing features of the *endocarditic group* are: The earlier age, the absence of involvement of the root of the aorta so that the coronary arteries are unimpaired, and the greater frequency of the combination of narrowing with stenosis, particularly in young persons. There is a very acute endocarditic-aortic insufficiency coming on in the course of a severe rheumatic endocarditis or in the ulcerative forms in septicemia, pneumonia, and gonorrhœa. Within a week, even within three or four days, the signs of aortic insufficiency may be well marked. In the rheumatic cases recovery may take place, but in the septic forms a malignant endocarditis is apt to develop.

2. **Syphilitic.**—In this, the insufficiency is part of a wide-spread arteritis or of a lesion limited to the root of the aorta. The segments really behave as portions of the aorta, and are involved with it in the degenerative changes. After forty, the aortic segments always show slight signs of wear and tear, and in hard drinkers and hard workers with syphilis the segments become involved also. The exceedingly delicate texture is lost, the edges curl, and the segments thicken, become foreshortened and so unable to come into close apposition during diastole. So slight is the alteration in some cases that the valves look almost normal, or there may be shortening of only one segment. The surface of the valves may be perfectly smooth, without calcifications or adhesions between the segments, so that there is no narrowing of the orifice. With this a varying degree of involvement of the arch of the aorta and of the vessels generally

is associated; sometimes the arch is in an advanced state of endarteritis deformans, greatly dilated, with depressed scars and even aneurismal. But in other instances the valves themselves show relatively more disease than the aorta. The orifices of the coronary arteries are involved, usually narrowed by the endarteritis, or the branches of the vessels themselves may be diseased. This is the common type met with in hardworking men between forty and sixty, without any history of rheumatism.

It may occur in young men within two or three years from the date of infection. It is associated with a syphilitic mesarteritis of the root of the aorta, which may directly implicate the adjoining segments. It may come on with severe pain, frequently anginal in character. Sudden death may occur from the involvement of the coronary arteries. The insufficiency gradually develops under observation. In other instances, with appropriate treatment, the condition improves and the case finally settles into one of chronic aortic insufficiency.

3. Arteriosclerotic.—A *senile* type of aortic insufficiency is not very infrequent. Met with in men over seventy it is due to a gradual thickening, calcification, and adhesion between the segments, so that there is narrowing of the orifice and slight permanent insufficiency.

4. Relative Insufficiency.—Corrigan recognized this in his original paper, and stated that without any organic lesion of the segments, insufficiency might be caused by dilatation of the aortic orifice. Discussion has taken place as to the existence of this form. While rare, there can be no question of its occurrence. Most experienced clinicians have observed rare cases in which aortic regurgitation has been temporary. Experimentally it has been produced by section of certain muscular strands. It may occur with diffuse dilatation of the aorta.

5. Rupture of a Valve.—This rarely happens to a healthy valve, but it has been quite frequently met with in disease following the strain of a sudden exertion upon segments already diseased or the seat of endocarditis. Still more often it has followed trauma, a kick from a horse on the chest, or a fall. One or two valves may be involved. It is more frequent in the aortic than in the other valves. Of 72 observations collected by Dreyfus, 46 were of the aortic segments.

6. Congenital.—A considerable number of cases are due to congenital malformation of the segments, resulting in a fusion of two of the cusps, and almost invariably those behind which the coronary arteries are given off. Of 17 cases, all of which presented sclerotic changes, the majority had had during life the clinical features of chronic heart disease.

Circulatory Adjustments.—The abnormal features are the hypertrophied heart, the collapsing pulse, the capillary pulse and the pallor. The prevalent views of the condition of the heart and bloodvessels in aortic regurgitation require modification. It is commonly held that with a defect in the valves a large amount of blood flows back into the ventricle from the aorta, and that the distention thus produced in diastole has a greater tendency than normal to distend the chamber. Stewart¹ showed that the quantity regurgitated, except in very marked degrees of

¹ *Arch. Int. Med.*, 1908, 1, 1.

the condition, is not more than a small fraction of the total amount of blood in the ventricle. The effect of the regurgitation is to counterbalance the negative pressure present in the chamber immediately after systole and to put a positive pressure in the ventricle in all periods of diastole. The effect of this positive pressure is to cause an increased tone of the ventricular muscle, as can be shown by comparing the volume curves of the heart in the normal animal and after the production of regurgitation. The probable explanation of this is that the cardiac muscle in aortic regurgitation is "overloaded," for Stewart determined that the summit of the curve occurs after that of the normal. He showed, moreover, that the collapsing pulse is not due to regurgitation into the left ventricle, but to a reflex dilatation of the peripheral arterioles from stimulation of the ventricular wall by the increased pressure. In some of his experiments, when the operation failed to produce the lesion of the aortic valve, nevertheless, as a result of touching the ventricular wall, the typical features of aortic regurgitation were evident in the records. Stewart explained this reflex as the normal means of preventing the effects of undue pressure in the cavities of the heart. The collapsing pulse in experimental animals is changed to one that is more normal by increasing the peripheral constriction, as, for instance, by compressing the abdominal aorta or by injecting epinephrine; this is confirmed by finding that compression of the vascular area peripheral to the radial artery in a case of pure aortic regurgitation produces the same result. This fact, the low peripheral resistance in aortic regurgitation, is probably the reason for the frequent presence of capillary and sometimes even venous pulsation. Lewis and Drury, however, in a recent paper¹ support the original view that the condition in the arterial system is due to the leak of blood back into the ventricle, supporting their view by reference to the disappearance of these features in arterio-venous aneurism by cure of the aneurism.

The *Corrigan pulse* is more marked when the radial artery is felt with the arm held vertical. This is probably not due to the accentuation of regurgitation, but to the diminished venous pressure and consequent greater capillary flow; for if in this position the veins be constricted the collapsing pulse tends to disappear. A slowing of the heart beat of itself is probably not harmful if tonus is well maintained, because the volume curves in experimental animals show no greater filling of the ventricle during vagus stimulation than before.

The blood-pressure in aortic regurgitation shows very constant features in experimental animals. The systolic blood-pressure remains the same within very narrow limits, the diastolic is invariably lessened, and therefore the pulse-pressure is increased. In man the maximum pressure is usually raised, very rarely normal; the minimal pressure is always less than normal. The blood-pressure in the leg arteries is in excess of the brachial—a point which may be used in differential diagnosis, as it is not known to occur in other cardiac cases.

To the extra amount of blood which the left ventricle holds at the end of diastole is due (from increased stretching) the hypertrophy

¹ *Heart*, London, 1923, 10, 307.

which follows aortic regurgitation. If the insufficiency is small, then perhaps the cavity is not dilated sufficiently to give any change in the bulk of the left ventricle; hence occasionally a slight amount of aortic regurgitation may be present without any obvious enlargement of the heart (Krehl). When slight regurgitation is present, even though hypertrophy is marked, compensation may be maintained for many years, as may be seen in aortic regurgitation from rheumatic endocarditis. The hypertrophy while affecting mainly the left ventricle also affects the right ventricle (Lewis.) In a pure valvular lesion, which can, however, seldom be supposed in rheumatic cases, the limits of cardiac reserve power are little if at all lowered.

Symptoms.—These are best considered under certain groups of cases:

1. **Latent.**—It is surprising how often in the routine examination one meets with aortic insufficiency that has never caused any symptoms. Even in quite young men with no history of rheumatic fever the condition may be detected accidentally, as in the examination for life insurance. Such patients may continue for years doing the ordinary work of life without the slightest inconvenience.

2. **Acute Aortic Insufficiency.**—In rheumatic fever, in septic conditions, and following a trauma, acute insufficiency may arise. The general features of endocarditis are usually present, fever, sweats, etc. There may be nothing to attract attention to the heart itself. Palpitation or tumultuous action may be complained of, and occasional pain. As the condition grows worse there may be attacks of oppression of breathing, and even dyspnœa, but it is surprising, even in severe cases of ulcerative endocarditis, how slight may be the symptoms pointing to the heart. The physical signs are usually well marked—the rapid, forcible action, the throbbing vessels, and, under observation, the signs of insufficiency may increase. In some of the rheumatic cases it may be months before the compensation is established and the patient is able to get up and move about comfortably and take exercise without shortness of breath. Even in cases that look the most hopeless, with extreme insufficiency, the severe features may gradually subside. One friend whose life was despaired of in 1884, in his second attack of rheumatic fever, survived and practised medicine for nearly twenty years. In other cases the acute insufficiency results from rapid destruction of the valve segments in a septic endocarditis, and the picture and course are those presented by this disease.

Some of the cases of the *syphilitic* aortic insufficiency come in this category. The patients are young men, and within a year or two of the primary infection, usually with the symptoms of angina pectoris, the aortic insufficiency develops in connection with a localized arteritis at the root of the aorta. The symptoms may disappear with antisiphilitic treatment, but the senior writer did not see an instance in which the murmur of aortic insufficiency disappeared.

3. **Cases with Broken Compensation.**—For years before the breakdown occurs the patient may present a suspicious pallor of the face, the so-called aortic facies. Pronounced vertigo, or on exertion a ringing in the ears, may recur at intervals for months. Shortness of breath on

exertion, attacks of nocturnal dyspnœa, uneasy fluttering sensation about the heart, or attacks of palpitation may initiate the breakdown. The pulse becomes somewhat rapid, is feebler, and sometimes irregular; the respirations increase; there are signs of congestion at the bases of the lungs, the liver may be enlarged, and the signs of venous stasis gradually develop; there may be slight œdema of the feet, but general anasarca is rare. The breakdown may be associated with attacks of cardiac pain, anginal in character. Some of the old hospital patients are admitted ten, fifteen, or even twenty times, always with the same symptoms, shortness of breath, cough, signs of engorgement at the bases of the lungs, albuminuria, and perhaps slight œdema of the feet. In some cases there is marked anemia. Dyspeptic symptoms are common, and the attack may begin with nausea and vomiting, which may remain troublesome features throughout. *Mental symptoms* are perhaps more commonly met with in aortic insufficiency than in any other form of heart disease. Delusions may occur even without any loss of compensation. More frequently with the breakdown, the patient begins to lose his mental control, and all sorts of delusions arise, particularly relating to time and place. In the endocarditic form, seen most frequently in young people and often in combination with a mitral lesion, the picture may be that of a gradual failure with venous stasis and dropsy.

Fever, when present, usually indicates either a recurring endocarditis of the sclerotic valves or the presence of a complication.

Physical Signs.—Inspection.—Aortic insufficiency is the only valvular lesion which we can recognize at sight. There is no other condition with which so distinctive a type of throbbing of the arteries is associated. The beating of the carotids above the collar, the visible throbbing in the peripheral arteries, such as the radials and the temporals, and, on ophthalmoscopic examination, the retinal arteries. The peculiar jerk of the foot when the knee is crossed may suggest the diagnosis. Even the head may jerk with each systole. There are one or two conditions which simulate it, which will be referred to later.

Heart.—In children and in young persons the precordia may bulge. In the syphilitic variety there is rarely any deformity of the chest. As the left ventricle reaches a very large size, the apex beat is dislocated downward and outward and is usually in the sixth interspace, sometimes in the seventh, and 1 inch or even 2 inches outside the nipple line. With full compensation it is regular, forcible, often punctuate, but when dilatation is extreme the impulse is diffuse, often wavy. Although the heart is large, and, as seen by the fluoroscope, low, it is very rare that pulsation occurs beneath the costal border in the nipple line. Localized pulsation may be present at the ensiform cartilage and there may be a diffuse impulse extending up the left of the sternum. In children the action of the heart may be very tumultuous. In ordinary cases no pulsation is visible at the base, but with extreme anemia or when the insufficiency has been rapidly produced, as in ulcerative endocarditis, there may be remarkable pulsations over the aorta and extending into the neck and along the course of the subclavian arteries. These are the cases in which, as Corrigan observed, the diagnosis of aneurism is usually made.

Arteries.—By inspection of the arteries alone the diagnosis may often be made. The subclavians and carotids throb violently, and there may be a visible pulsating tumor above the sternal notch. The brachials are visible, sinuous in their course, and with each systole they expand rapidly and as quickly collapse. Similar large pulsations may be seen in the radials and the temporals and even in some of the smaller vessels. In no other state do we see such widespread and peculiar throbbing in the peripheral arteries. Occasionally this diffuse vascular impulse is evident in the solid organs, as the liver and spleen, in which a pulsation may be felt, and the whole pharyngeal region may throb visibly and change in color with each systole. The beating in the retinal arteries may be forcible and even be distressing to the patient.

Capillaries.—The capillary pulse, first pointed out by Quincke, is seen in a great majority of cases. Capillary pulsation is frequently seen in other conditions in which there is vasodilation, as in warm weather or after a hot bath. It may be looked for on the nails, or a line may be drawn on the skin, or it is well seen by the pressure on a bit of glass upon the lip. The finger nail is a very satisfactory locality to see it, but it requires good eyes and always good light. Occasionally it is present in a very remarkable form. The palms of the hand blush with each systole and become pale in diastole. Held up against the light the change in color of the skin may be visible 6 or 8 feet away. In some cases the length of the tongue when the mouth is open may be seen to increase at each systole.

Veins.—Pulsation in the cervical veins is common, but it may be difficult to distinguish from the communicated throbbing of the violently beating carotids. The superficial veins are often very full, and it is one of three or four conditions in which pulsation is common, particularly on the back of the hand and in the veins of the arm.

Palpation.—Depending upon the stage of the disease, the cardiac impulse is felt to be forcible, punctuate, heaving at the apex, or, when compensation fails, widespread, wavy, and diffuse. The whole front of the chest may be lifted during systole of the huge heart. The shock of the sounds at the apex is occasionally felt. A systolic thrill is rare at the apex. A thrill is sometimes present with the qualities of the mitral presystolic thrill, and it may even terminate abruptly in a first sound. In the endocarditic form, with an associated stenosis, a thrill is not uncommon at the base, usually systolic, but sometimes double. A marked diastolic thrill may be caused by a calcified spur in the valve.

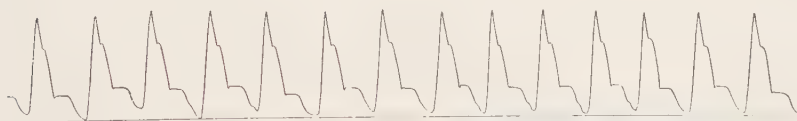
The *arteries* feel large and are frequently sclerotic. From the character of the pulse alone the diagnosis may be often made. Even the handshake may suggest the lesion, or the characteristic quality may be perceived by touching the foot of a patient as he rests in bed. The pulse beat (*pulsus celer*) is sudden, forcible, and then drops immediately, resembling the beat of a water-hammer (water-hammer pulse). The abrupt shock-like sensation communicated to the finger is followed by a sudden collapse—hence the name *collapsing pulse*. By elevating and grasping the arm about the middle, the palm of the hands toward the radial and ulnar arteries, the jerking quality is best perceived. It may be felt in the finger tips and even in the toes. The hand laid upon the

dorsum of the foot may feel it with great distinctness. With anemia it becomes very marked. The pulse is regular, except during certain complications and toward the close when the heart muscle fails. The sphygmographic tracing in marked cases is very characteristic—a straight and high line of ascension showing the abrupt and forcible distention of the artery, a rapid line of descent forming a very acute angle with the upstroke.

A thrill may sometimes be felt over the larger vessels. At the root of the neck the arteries may feel very voluminous, and even in diastole may be so distended, particularly in young persons, that the diagnosis of aneurism is made.

Auscultation.—A diastolic murmur is heard at the base of the heart, of maximum intensity over the sternum opposite the second or third interspace, sometimes at the left border of the sternum at the third or fourth costal cartilage. It is sometimes better heard if the patient leans forward. Authors differ very much in assigning the point of maximum intensity to this murmur. The French, particularly, place it at the right border of the sternum. The truth is it varies greatly in different cases. In the endocarditic form and when stenosis is present the murmur may

FIG. 37



Aortic regurgitation. The pulse tracing shows a rapid rise and fall.

be most intense at the aortic cartilage. In the arteriosclerotic form, particularly when the murmur is soft, the maximum is more commonly at the left border of the sternum in the third or even the fourth interspace. The variation has been thought to depend upon the position of the insufficient segment. No murmur may be present to the right of the sternum in the situation at which one usually listens. The murmur may be so soft as to be readily overlooked, or it may be rendered audible only by exertion. A diastolic murmur may disappear under observation, or it may change its character. In a few cases, though insufficiency is present, a diastolic murmur is not heard. In personal experience this has been very rare, but it may occur in the arteriosclerotic form. On several occasions the senior author heard a soft diastolic murmur, when postmortem, the valves by the water test appeared to be competent; but in these cases the segments were a little sclerotic, and there may have been dilatation of the aortic ring.

The *quality* of the diastolic murmur varies greatly in different cases. It may be a soft-drawn murmur, only just audible, or an intense blowing murmur, while in other cases it has a musical quality. In a majority of the cases there is a double murmur; in the endocarditic form the systolic is usually rough and rasping in quality, in the arteriosclerotic

it is soft. A systole bruit is not always present. The normal aortic second sound may be audible, but in a majority of cases it disappears altogether. The murmur is propagated down the sternum, and may even be intense at the ensiform cartilage. As a rule, it is not audible beyond the left parasternal line at the level of the fifth rib. In the common cases of the syphilitic form it is not heard up the sternum or in the vessels of the neck. When there is dilatation of the aorta and much roughening of the intima, the diastolic murmur may be well heard at the base of the sternum and in both carotids. So also the loud rough, systolic murmur in connection with aortic stenosis may be transmitted upward. Change in posture does not, as a rule, make very great difference, except intensifying the murmur. Occasionally the alteration from the recumbent to the erect position may bring out a musical quality.

A systolic murmur of mitral insufficiency is present with the combined aortic and mitral lesions in the endocarditic group, particularly in children; in the arteriosclerotic group when the mitral segments are themselves curled and shortened, and with great dilatation of the ventricle when relative insufficiency of the valve occurs.

The electrocardiogram in aortic regurgitation tends to show a flattening or an inversion of the *T*-wave.

The Apical Diastolic Murmur (the Flint Murmur).—In a majority of cases of aortic insufficiency, a murmur is heard in the apex region with a rumbling, purring quality, at once suggestive of the one heard in mitral stenosis. Austin Flint first described this murmur and it has been studied with great care by numerous observers. The results of the Johns Hopkins Hospital studies were published by Thayer.¹ The murmur is common, being heard in slight grades in a majority of cases. It is apical in situation, usually above and to the inner side of the maximum apex beat. It is often very localized. It may occur throughout the entire diastole or through the terminal portion, being purely presystolic, or in some instances distinctly mid-diastolic. The striking feature is its rumbling and vibratory quality, such as is so distinctive in the presystolic murmur of mitral stenosis. Sometimes there is a crescendo character, and it may terminate abruptly in a sharp snapping first sound. When to these features are added a thrill and a shock of the first sound felt on palpation, it is not surprising that the diagnosis of mitral stenosis is made. Time and again under these circumstances we have discussed the possibility of the existence of mitral stenosis, every cardiac physical sign of which was present. This difficulty is apt to occur in young persons with the endocarditic form, in whom the possibility is always present of the involvement of both orifices. In the subjects of syphilis and in the arteriosclerotic form the chances are always against mitral stenosis, even with a combination of physical signs which almost compels the diagnosis.

Auscultation of the Arteries.—Along the subclavians and carotids the diastolic murmur may sometimes be heard. Occasionally the double murmur is transmitted. As a rule, in the arteriosclerotic form the diastolic murmur is not heard above the level of the second costal cartilage,

¹ *Amer. Jour. Med. Sci.*, 1901, **122**, 538.

and is not transmitted into the arteries. The most characteristic phenomenon over the larger arteries, particularly the femoral, is the "pistol-shot" sound, a short, sharp systolic shock, and, as Traube pointed out, a second sound feebler than the first, coincident with the diastole of the artery. The latter is not always heard. With very slight compression of the artery, particularly at the femoral, a double murmur is heard — Duroziez's sign.

Diagnosis.—No heart affection is so easy to recognize, and there is none so frequently overlooked. The diastolic murmur, and the visible collapsing pulse are pathognomonic. The mistake most likely to arise is the one mentioned by Corrigan in his original paper, namely, the diffuse throbbing of the aorta and the large vessels suggest aneurism. A diastolic murmur at the base is heard in several other conditions. Insufficiency of the pulmonary valves occurs in a few instances in connection with long-standing mitral disease. The conus arteriosus and the ring of the pulmonary artery are dilated, and there is relative insufficiency of the valve. The murmur is sometimes called after Graham Steell, who called special attention to this lesion. It is more often diagnosed than existent. In several cases in which we thought it to be present in young persons the lesion proved to be aortic. The situation in the left intercostal space close to the sternum is of no moment whatever, as this is a common situation for the aortic diastolic murmur. The two important points really are the existence of old mitral disease and the absence of the characteristic vascular phenomena of aortic insufficiency. A diastolic murmur heard over the sternum may be of venous origin, and is met with particularly in Graves' disease. Cases have been described, too, in young persons in whom no definite cause could be assigned. Some of these cases may have been due to pressure of glands on the veins. Occasionally the *cardio-pulmonary* murmurs are diastolic, and to this class in all probability belong the so-called transitory diastolic murmurs which are reported at intervals in the literature.

Rupture of the valve is indicated by a sudden onset after exertion, with pain, tumultuous action of the heart, and a loud, perhaps musical, diastolic bruit. The arteriosclerotic form is rare under thirty-five years of age. It is associated with signs of arterial disease, and the etiological factors are drink, hard work, and the stress and strain of life, or syphilis. Endocarditic cases occur in the young with a history of rheumatism or of some severe infection. More frequently than in any other form the orifice is narrowed, and there is a loud, rasping, systolic bruit. Relative insufficiency occurs in connection with dilatation of the aorta or with aneurism. The murmur is usually soft, and it may be heard high on the sternum, and with extreme atheroma a systolic murmur is usually present. In very old persons the insufficiency and stenosis are usually combined, and there is a rasping systolic murmur with a thrill.

Special Features and Accidents of the Disease.—Aortic insufficiency is a disease of accidents and surprises. Sudden manifestations may occur after a long period of latency. Among these the following are the most important: (1) The sclerotic aortic valves may be attacked by *endocarditis*, which may assume the ulcerative form. (2) In the sclerotic

variety, in which the root of the arch and the coronary arteries are very apt to be involved, *angina pectoris* is common and death may occur in the first attack. In the syphilitic form, recurring attacks may precede the insufficiency, the process of which may be gradually traced. (3) *Sudden death* is more common in aortic insufficiency than in any other valvular disease. It may occur while the patient is at rest, even while asleep; more frequently it follows a sudden exertion or a violent emotion. While it may be due to acute dilatation, it is more probable that in a considerable proportion of the cases the coronary arteries are involved and there is a sudden interference with the circulation of blood in the heart muscle itself. (4) *Embolism* is not so common as in mitral disease. A vegetation growing on the sclerotic valves may be dislodged and plug a cerebral vessel, or a calcified fragment or an atheromatous flake may become detached and pass to the brain or to one of the peripheral arteries. In one instance the formation of a popliteal aneurism followed the dislocation of a fragment from the valve, which had been associated for years with a musical diastolic murmur. Following the accident the quality of the murmur changed entirely.

Prognosis.—Recovery is stated to occur, even by observers so careful as Potain, Leyden, and Gerhardt. The diastolic murmur in rare instances disappears, but in the event the regurgitation is probably from a dilatation of the ring. It is highly improbable that regurgitation from a sclerotic valve can ever disappear. It does not seem likely, as has been suggested, that when only one valve is affected the other two could enlarge and so compensate for the defect. The prognosis varies with the different varieties. The endocarditic is the most hopeful, except in young children with a combined mitral lesion; but in young men compensation may be perfect, and for years there may be no symptoms. After an active life the patient may reach a good old age. Recurrent endocarditis, the chronic septic form or the rheumatic variety, may attack the valves, but such a patient may go through serious illness, even severe rheumatic infections, and recover with a useful heart. In the syphilitic form, the prognosis is bad, unless an early diagnosis is made and prompt treatment given. Even adequate treatment in those cases in which considerable damage has been done, can only alleviate. In the arteriosclerotic form the regurgitation is seldom of a serious grade.

Both in the young and in the aged, moderate stenosis lends a rather more favorable prognosis to the condition. Combined with mitral insufficiency, due to disease of the valve, the outlook is not so good. In adults, slight relative insufficiency of the mitral is a favorable feature.

STENOSIS OF THE AORTIC ORIFICE.

This is the rarest of all forms of valvular disease, and usually with it is associated some grade of insufficiency.

Incidence.—In the Edinburgh Infirmary Statistics, it occurred alone in 40 cases out of 1911, and in 152 cases with another lesion. Among 670 cases of valvular disease Romberg found only 28, among which there were only 17 without simultaneous disease of other valves.

Etiology and Morbid Anatomy.—As a rule, the process is chronic, but in a few cases one meets with an acute stenosis due to the growth of very luxuriant vegetations on the valves. There are two great types of the disease, the endocarditic and the arteriosclerotic.

Following *endocarditis* from any cause, but more particularly from rheumatic fever, the vegetations organize, the edges of the valve thicken, become adherent, sclerotic, and finally calcareous. The segments may be infiltrated with lime salts, and even the aortic ring itself, the whole forming a rigid, calcified mass perforated at one spot by a rounded, oval, or linear orifice. Very varying degrees of involvement of the segments are met with. As a rule, they are greatly deformed, but sometimes only the margins are diseased, and the narrowing results from the calcified nodular outgrowths. Indeed, Rendu, quoted by Barié, reports a case in which the narrowing was due to an enormous hypertrophy of the nodules of Arantius. The degree of stenosis is very variable, and may reach a remarkable grade, so that the orifice is not more than a few millimeters in diameter. Insufficiency is always present, the degree depending on the size of the orifice. Of course, when there is calcification and rigidity, there is no possibility of closure of the orifice during diastole. In this endocarditic form the aorta itself is not involved.

In the *arteriosclerotic* type the lesion of the valve is part of a widespread arterial degeneration. In men at the middle period of life the sclerosis is not often associated with stenosis. Occasionally there is a slight grade, but one may examine anatomically 25 or 30 cases of sclerosis of the aortic valves in succession without any narrowing of the orifice. In a few cases the edges of the valves coalesce and some narrowing results from atheromatous changes with calcification. The most characteristic form of arteriosclerotic stenosis is seen in elderly persons. It comes on insidiously, and may attain a very pronounced grade without causing any symptoms. In a special variety, described by Norman Chevers, the stenosis does not involve the ring, but the infundibulum or the part below it. This usually follows an extension of a chronic mitral fibrosis.

The heart is enlarged, sometimes very greatly, but rarely reaching the size of that of pure insufficiency. Early in the disease there may be pronounced hypertrophy without much dilatation, and clinically the enlargement may not be very great. Theoretically, with an obstruction at the aortic orifice, the ventricle is unable to expel the usual amount of blood into the aorta. The cavity at the beginning of diastole still contains blood, so that at the beginning of systole it is fuller than normal. This causes a greater stimulation of the muscle fibres of the walls, more pressure per unit area is exerted on the contained blood, and more is forced into the aorta through the obstruction. The stimulus of a resistance to contraction during its activity, *i. e.*, when the muscle is overloaded, causes systole to be prolonged from 7 to 30 per cent. of the normal. This differs from aortic regurgitation, in which the systole is little if at all prolonged. In this, however, there is no extra resistance to contraction during the period of activity. If the extra force expended by the ventricle is sufficient to discharge the normal amount of blood into the aorta, the cavity is not increased in size, and with the development

of hypertrophy the circulation goes on as before. But if the stenosis is greater than can be overcome by the ventricle, or if the muscle of the ventricle is enfeebled, there is residual blood at the end of systole and the ventricular cavity is permanently enlarged. A third stage is that in which not only the ventricle but also the left auricle is overfilled at the beginning of systole. The auricle, by increasing the vigor of its contractions, may for a time be able to cope with it, but further failure may set in, leading to the same series of changes as occurs in mitral disease—congestion of the lungs, hypertrophy followed by failure of the right ventricle, venous engorgement, and œdema.

The estimation of the blood-pressure in aortic stenosis shows that little if any difference exists from the normal. The number of recorded cases is, however, not great. We should expect to find that the maximum and minimum pressures were nearer one another than in a normal person.

Symptoms.—No heart lesion is more frequently latent. In the arteriosclerotic form, years may elapse before the patient experiences any discomfort. Indeed, it is one of the diseases, to use an expression of Oliver Wendell Holmes, that may promote longevity. It has helped many a man to become an octogenarian. In young persons, following endocarditis, symptoms on the part of the heart are more frequent—palpitation, irregularity, distress on exertion, and the cardiac reserve is readily exhausted. It is not always easy to separate the effects of the aortic from the mitral disease, if present. In old persons, vertigo is a common symptom, and shortness of breath on exertion. An extraordinary degree of muscular vigor and good health may be maintained, but the capacity for exertion is greatly reduced, and breathlessness follows any extra effort. Attacks of angina occur in some cases, in one of which death may take place. Many patients have a sense of oppression and distress beneath the sternum on the slightest exertion or emotion. Cardiac failure may occur with venous stasis and all the signs of cardiac dropsy. Sudden death is not very uncommon.

Physical Signs.—**Inspection.**—In young persons the precordia may bulge and signs of hypertrophy are present. In these cases the degree of enlargement of the heart depends much more upon involvement of the mitral and the amount of insufficiency of the aortic cusps. When these are present, there may be a great deal of dilatation and a very large heart. On the other hand, with pure stenosis there may be little or no hypertrophy, and the apex beat may be dislocated a little down and out, but the organ is not greatly enlarged. The apex beat is usually felt in the fifth or sixth interspace, forcible, and regular. Traube pointed out that in a considerable number of cases the apex beat was absent.

Percussion. Percussion shows slight increase of the cardiac dulness downward and to the left, varying with the degree of dilatation. On *palpation*, a systolic *thrill* is felt at the base, a maximum intensity in the second right intercostal space and sometimes felt in the carotids and subclavians. On *auscultation*, a loud, rough systolic murmur is heard, of maximum intensity at the base. It is harsh, rough, rasping, usually protracted; in other instances high-pitched, whistling, and musical. It is propagated along the vessels of the neck and along the subclavians.

It is sometimes heard with great intensity toward the apex of the heart, even when there is no mitral disease. The first sound is usually absent or very feeble. The second aortic sound is, as a rule, absent or replaced by a diastolic murmur, of varying intensity and quality. Sometimes the second sound is quite well heard, but it depends on the measure of retention of the elasticity of the aortic segments. It is not probable that with uniform calcification and rigidity, any sound could be produced. A peculiarity, more common in aortic stenosis than any other valvular lesion, is the murmur audible at a distance from the chest wall. This was noted by Stokes in the case of a politician in whom the murmur was so loud that it could be heard by his colleagues sitting about the table. The *pulse* is slow, small, hard, and regular. The rate does not often fall below 60, and occasionally it is permanently at 40. In the senile cases, the Stokes-Adams syndrome may be present, and syncopal attacks or epileptiform seizures occur. The pulse is small, because the orifice permits of a comparatively small amount of blood, and the smallness of the beat may contrast in a striking manner with the force of the cardiac pulsation. Hardness is, as a rule, associated with the sclerosis of the vessel. Tracings are very characteristic, and show a small pulse wave, with a rounded or flattened summit, with a very oblique line of ascent, and almost without dicrotism.

Diagnosis.—The disease is frequently diagnosed when it does not exist. To inexperienced observers any loud murmur at the base suggests stenosis, whereas that lesion is the last to be considered. Slight roughening of the valves, roughening of the intima of the aorta, and hemic conditions are common causes of the systolic murmurs at the aortic area. With aneurism, too, a loud murmur is occasionally present. Stenosis of the pulmonary orifice has very much the same features on palpation and auscultation, but it occurs, as a rule, in young persons, the murmur is not propagated to any extent into the vessels of the neck, and is loudest to the left of the sternum.

Prognosis.—In young persons it is bad, particularly with associated mitral disease. Sometimes in the pure aortic stenosis following rheumatic fever the compensation may be maintained for many years, but, as a rule, the outlook is not so good as in the late sclerotic form of insufficiency. In any case, it is a lesion that takes many years for its formation, and many patients succumb to accidents, not to the disease itself. The most favorable cases are those in which, as a result of a slow, presenile sclerosis the orifice has been gradually narrowed. If the patient accepts the conditions, lives a peaceful, easy life, the heart lesion itself may promote longevity. For many years the senior writer followed with interest the lives of two old men with typical features of aortic stenosis. One was an Anglo-Indian who lived to be over ninety years of age. He had a very large heart and a thrill at the base which could be felt through his overcoat and the murmur was audible some distance from the chest wall. The other died at the age of ninety-two years, of bladder complications. The patient was about sixty years of age when the aortic stenosis was diagnosed by Walshe.

Loss of compensation is usually the result of myocardial changes, and once gone is rarely restored.

INSUFFICIENCY OF THE MITRAL VALVES.

When from any cause the mitral segments do not close during systole of the ventricle a variable, amount of blood passes back into the left auricle through the insufficient valves. This is one of the most common of all cardiac lesions. In the Edinburgh figures, among 1914 cases there were 585 with mitral insufficiency alone, and 463 in which it was combined with another lesion, 231 this being mitral stenosis.

Forms.—There are three great groups of cases, the *endocarditic*, the chronic *sclerotic*, and the *relative* or muscular. In a few cases the insufficiency may follow rupture of one of the segments.

Endocarditic Form.—This, the most common, is met with in young persons as a complication of the acute infections, more particularly of rheumatic fever. The general effect of endocarditis upon the valves has already been described. The special danger of the rheumatic form is owing to the fact that the segments are the seat of a productive valvulitis. In certain cases, insufficiency is rapidly produced by destructive lesions which erode the chordæ tendineæ and destroy the segments, so that within a week or ten days a high grade of insufficiency is produced. In a large proportion of all cases there is no actual erosion of the valve itself, but the insufficiency is caused by a gradual shrinkage of the newly formed connective tissue in the substance of the valve. When this goes on very rapidly, as is sometimes the case, both curtains are rolled up as it were, leaving a widely open orifice. This is not nearly so common as the slower process in which the constricting cicatrization draws together the margins of the valves, so that with the insufficiency there is some grade of narrowing. The orifice may admit the thumb, or not more than the tip of the little finger. The edges are smooth, greatly thickened, often of a cartilaginous hardness, and the chordæ tendineæ are greatly thickened, shortened, and often fused together. It is quite frequent to have beads of fresh endocarditis on the margins of the thickened valves. Lime salts may be deposited, and the valves and ring together form a solid calcified mass.

Arteriosclerotic Form.—In this, without any preliminary acute endocarditis, the valves gradually thicken, the edges become curled, slightly shortened, the chordæ tendineæ become thickened, the orifice is slightly narrowed, lime salts are deposited in the valves, and, as age advances, the whole valve and ring become a rigid and calcified membrane. In a slight degree, sclerosis of the mitral valve is met with in all persons over sixty years of age, and is an expression of the wear and tear of work.

Relative Insufficiency.—Relative insufficiency, by far the most common form, occurs whenever dilatation of the mitral ring reaches such a grade that the normal valve segments are no longer able to close it. Known by the names of functional, muscular, or, more commonly, *relative* insufficiency, the most common cause is loss of tone of the muscle which surrounds the mitral ring. This occurs in many blood conditions, such as anemia, in fevers, in many neurotic states, as neurasthenia, in Graves' disease, and in all cases when the dilatation of the ventricle from any cause reaches a certain grade.

Insufficiency due to rupture of the chordæ tendineæ, or of one segment, is very rare in the healthy valve, but a number of cases have been described; most frequently the chordæ tendineæ of the anterior segment are ruptured.

Symptoms and Physical Signs.—Many patients with mitral insufficiency never present any symptoms. In a still larger proportion symptoms are only present at the terminal stage of a long and silent history. The cases which give rise to symptoms earliest are those of insufficiency following the endocarditis in children, particularly in the tragic group which makes rheumatic fever so malignant an infection. Relative insufficiency in the fevers or in anemia may never give rise to symptoms. No valvular lesion presents such diversity of features in regard to the duration and severity. There are cases in children in which the valve segments are rapidly curled and rendered so insufficient that the limits of compensation are quickly reached. On the other hand, there is no valve lesion in which we see more perfect and more enduring compensation. The marvellous manner in which the heart is able to carry on the work illustrates the remarkable response of muscle to calls made upon it very gradually. It reminds one of Montaigne's illustration of the force of custom: "He seems to me to have had a right and true apprehension of the power of custom, who first invented the story of a country woman who, having accustomed herself to play with and carry from the hour of its birth, a calf in her arms, and daily continuing to do so as it grew up, obtained by this custom that when grown to be a great ox she was still able to bear it."

Circulatory Adjustments.—Depending upon the degree of insufficiency of the valve, a variable amount of blood is forced back into the left auricle, during its diastole, and while it is filling from the pulmonary veins. With this extra amount of regurgitated blood the auricle reaches its normal distention sooner than previously. The pressure at the end of diastole is greater than at this period were there no valvular deficiency, the muscular fibres of the auricle are more stretched than normally, and the muscle is stimulated to a greater contraction. If the more powerful contractions, either immediately succeeding the lesion of the valves or ultimately by reason of hypertrophy, can force into the ventricle the normal amount plus the extra blood which was regurgitated, the circulation becomes compensated and the effects of the insufficiency do not extend farther than the left auricle.¹ Over and above the evidence of regurgitation by auscultation, very careful percussion may give a higher pitched note at the apex of the left lung in front, and with the roentgen-rays a marked increase in the amplitude of pulsation in the position of the left auricle may be seen. The electrocardiogram shows a more marked *P*-wave, sometimes with a broad or notched summit in Lead II; this wave disappears in auricular fibrillation. The left ventricle must accommodate the additional blood from the auricle, and in consequence its cavity becomes larger, its pulsations (owing to the slight stretching) more forcible, and hypertrophy of the muscular walls follows.

¹ C. J. Wiggers and H. Feil, *Heart*, London, 1921-1922, 9, 149.

In the condition just described it has been assumed that the normal closure of the pulmonary veins took place during the systole of the auricle. We do not know at present how this is accomplished, but from the analogy of the right auricle, in which muscular bands are disposed to that end, we may conclude that it is effected by the same process.¹ With further dilatation of the cavity, the orifices will remain open during the systole and the heightened pressure will be communicated to the blood in the pulmonary vessels. The dilatation of the auricle does not go beyond a certain point, partly because of the opening of the orifices of the pulmonary veins and partly from an increase in the connective tissue, which has been shown to accompany compensatory hypertrophy.

MacCallum and McClure,² in studying the effects of artificial lesions of the mitral valve in animals, have found that the pressure in the systemic arteries falls markedly, that in the left auricle rises, and that in the pulmonary artery may rise or fall; a high degree of insufficiency produces a fall of pressure in both the systemic and pulmonary systems; in slight insufficiency it usually rises. Whatever the pressure, the lungs invariably contain a larger amount of blood, for the venous pressure falls with a fall in the arterial pressure. The depletion of the systemic arteries is made up either by a constriction of the peripheral vessels, or by an increase in the volume of the blood.

In what way the hypertrophy of the right ventricle helps is an open question. MacCallum and McClure have shown that, so far as the pressure is concerned, the lung capillaries may be looked upon almost as a rigid tube, for the pulsations of the left ventricle are transmitted directly to the pulmonary artery, and with such little loss of time that the pressure wave of the left ventricle is opposed to the action of the right ventricle during the systole.

A mitral insufficiency compensated for ordinary conditions by the right ventricle may continue for a long period of years. If this chamber fails either from increasing deficiency of the mitral valve or from changes in its muscle, the tricuspid valve becomes incompetent. The right auricle becomes dilated and hypertrophied. The orifices of the veins are no longer closed during systole, and finally the pressure from the right ventricle is communicated to the venous system which becomes engorged. With great insufficiency of the mitral valve considerable pressure is communicated during systole to the auricle, whose walls probably become so stretched that the muscular fibres are injured and the contractions become very feeble. The increased pressure in the auricle and pulmonary bloodvessels gives rise to the thickened endocardium, so frequently seen in the former, and atheroma in the latter. In the first stage the left ventricle hypertrophies as a result of the increased pressure and compensatory dilatation at the end of diastole, caused by a more vigorous left auricle. Even with failure of the left auricle the pressure in it communicated from the right ventricle is sufficient to maintain the filling of the left ventricle, the hypertrophy of which may keep pace

¹ Keith describes a very probable method of closure of the orifices of the great veins into the right auricle, *Lancet*, 1904, i, 555.

² *Johns Hopkins Hospital Bulletin*, 1906, 17, 260.

with the further dilatation, and it may become very large and thick. Under these conditions the normal filling of the arteries would be maintained, but with failure of the hypertrophy and loss of the contractile power of the muscle, the arteries become less well filled and the blood-pressure tends to fall. With the lessened blood-pressure comes an increase in the rate of the pulse. The irregular pulse seen in the later stages of mitral regurgitation is usually due to auricular fibrillation.

Little can be said of the blood-pressure in mitral regurgitation. The condition of the pulse is no evidence of the height of the pressure for cases are recorded with a blood-pressure of 140 mm. Hg., in which the pulse was scarcely to be felt. With any irregularity of the pulse the maximum blood-pressure varies much, sometimes being only a little over 100 mm., at other times reaching 140 mm. or more. The feebleness of the pulse in mitral disease, when the pressure is high, may be due to peripheral constriction of small arteries to compensate for the underfilling of the arterial system, but of these peripheral mechanisms we have little knowledge.

Symptoms.—The symptoms may be divided into two groups. While compensation is still good, there are many minor manifestations, as the pain and breathlessness on exertion. When the insufficiency is extreme, the patients have a bluish tint of the cheeks and ears, giving the very suggestive appearance, the "mitral facies." The hands and feet may be blue, and in very long-standing cases the fingers may be clubbed.

Occasionally in children the degree of cyanosis reaches that met with in congenital heart disease, but it is never so extreme as in the cases of adhesive pericarditis with great hypertrophy of the heart and proliferative perihepatitis and peritonitis. Breathlessness on extra exertion may persist for years. These patients are especially liable to bronchitis in the winter. One of the most remarkable features is the recurrence, over long periods of years, of hemoptysis. In Philadelphia, the senior writer saw frequently a physician who had had his first attack of hemoptysis during the Civil War. Tuberculosis was then suspected, but a mitral lesion was discovered. On and off during twenty-five years he had had attacks of quite sharp hemoptysis, sometimes with great relief.

Broken compensation or decompensation may set in abruptly, following any extra exertion, a severe mental shock or a protracted illness. Palpitation, which objectively may have existed for years, becomes evident and distressing to the patient. The shortness of breath increases. The patient awakens at night, perhaps abruptly in a paroxysm of shortness of breath, or there may be distressing "sleep starts," in which, just as he is dropping asleep, he awakens gasping as though his heart had stopped. The most distressing single feature is the oppression in the chest associated with the breathing. The slightest exertion brings it on, and the patient may at last be unable to move from his bed, or the dyspnoea may continue even when he is at rest. Very soon the signs of venous stasis are present. There is oedema of the feet, which gradually extends upward; the abdomen begins to swell, the liver is enlarged, and there is slight jaundice. The anasarca becomes extreme and the serous sacs may become dropsical. The urine is scanty and albuminous, and contains tube casts and sometimes blood corpuscles. The patient is

restless, often sleepless at night, and there is anorexia and sometimes vomiting. With judicious treatment, even with rest alone, the attack may pass off, and months, or even years, may elapse before a breakdown occurs. Only too frequently once compensation has been broken, the patient is very liable to subsequent attacks.

Among special features which may be mentioned are embolism, either from a clot in the left auricle or from a vegetation on the edge of the thickened valves. A remarkable thrombosis may occur in the distended veins, particularly in the jugular or in the brachials. There was an extraordinary case at the Johns Hopkins Hospital—a woman who was under our care for many years. She had half a dozen attacks of thrombosis in different parts of the body.

A remarkable feature of these very chronic cases of mitral insufficiency is the recurrent *hydrothorax*, most common on the right side, which may be the only feature, and there are instances in which the patient has been up and about, and able to attend to his work, but has had to be tapped every week or even at shorter intervals. Perhaps the most extraordinary case on record of this kind is reported by W. T. Gibb, of New York; a physician with combined aortic and mitral disease was tapped 311 times in 580 days, but was able to be up and about and do almost anything, until two days before his death.

The *hepatic* symptoms of heart disease are met with in the most typical forms in mitral insufficiency. With the establishment of tricuspid insufficiency there is a swelling of the organ, the edge of which may be felt a hand's breadth or more below the costal border. On careful inspection, diffuse pulsation may be seen, and the organ may be felt to swell with each systolic impulse. A slight tinge of jaundice is common. In the long-standing cases, the liver becomes greatly enlarged, the connective tissue increases and the state of cardiac cirrhosis is gradually produced. The organ is large, smooth, and hard, with rounded edges. In very protracted cases shrinkage may occur. In an interesting group of cases for a year or more toward the close, the features are entirely hepatic and the patients come under observation with recurring ascites, which may require tapping every few weeks. The ascites may be the only form of dropsy present. While it is not always possible to exclude the influence of alcohol, yet there are cases in which the cirrhosis seems to be altogether a late effect of the stasis.

Physical Signs.—Inspection.—In children the precordia may bulge and there is usually a very large area of visible pulsation, undulatory along the left sternal border with a more definite apex beat in the fifth or sixth, sometimes the seventh, interspace. There may be visible pulsation to the right of the sternum and a marked impulse in the second and third left interspace. Frequently the whole front of the chest throbs visibly, and in mitral insufficiency we see more widespread impulse than in any other cardiac condition. The visible heart beat may extend from one anterior axillary line to the other. The impulse is usually very strong at the ensiform cartilage, and the heart may be so depressed and enlarged that there is a forcible, punctuate impulse of the right ventricle below the left costal border in the parasternal or even the nipple line. In the

arteriosclerotic type, in elderly persons, with very slight hypertrophy of the left ventricle, the impulse may be scarcely visible. In very long-standing cases, the apex beat may be far out, even in the mid-axillary line. In relative insufficiency, the impulse may be scarcely visible, and may be only a little, if at all, to the left of the nipple line.

The veins in the neck are usually full, and there are the pulsations described in connection with tricuspid insufficiency. In the stage of decompensation, at the jugular bulb, just above the right sterno-clavicular joint, there may be a large ovoid tumor as big as an egg.

Palpation.—The degree of shock will depend upon the extent and force of the cardiac impulse which may be very strong and heaving. A systolic thrill at the apex region is not so common as the presystolic in mitral stenosis, but in the long-standing cases in adults it may be very rough and rasping. The shock of a first sound is rarely to be felt, but the shock of the second may be widely diffused.

Inspection and palpation are the only safe guides in estimating the organic character of mitral insufficiency, if the apex beat is dislocated outward and very forcible, we may be certain that there is an actual lesion present.

Percussion.—The cardiac dulness is increased, particularly in a lateral direction, and may extend far to the right. The upper limit may be at the second rib, and in extreme cases far to the left, even to the mid-axillary line. Not even in the *cor bovinum* of aortic insufficiency do we find, particularly in children, such an extended area of cardiac flatness.

Auscultation.—A murmur accompanying or obliterating the first sound, of maximum intensity at the apex, and transmitted toward the axilla is the most distinctive single physical sign of insufficiency of the mitral segments. Its quality may vary from a soft blowing to a loud, harsh, rasping murmur; or it may have a distinctly musical quality, which is perhaps more frequently heard with mitral insufficiency than in any other lesions. The point of maximum intensity is, as a rule, at the apex or a little inside it. At times it is heard loudly along the right margin of the sternum and, as Naunyn pointed out, it may be even of maximum intensity at the second or third left interspace. The special direction of propagation is along the left pectoral fold into the axilla, and the murmur is often loud and distinct at the angle of the scapula. In long-standing cases with great hypertrophy the murmur may be heard all over the chest and even to the top of the head. With a murmur of any intensity the first sound is usually absent, but it is very variable and in many instances of relative insufficiency the first sound is well heard. The second sound at the base is greatly accentuated, particularly to the left of the sternum, over the region of the pulmonary artery. With failing compensation there may be a disappearance of the heart murmur and a confusion of sounds with the onset of fibrillation.

The *pulse* in mitral insufficiency in the stage of compensation may be quite regular, but in the endocarditic group in children and in adults irregularity is almost always the rule. For years it may persist without any sign of cardiac weakness and with a normal blood pressure, and even when the pulse is very small and extremely irregular the patient

may feel no inconvenience. The electrocardiogram will show that many of these irregularities are due to auricular fibrillation.

Diagnosis.—The recognition of mitral insufficiency is, as a rule, very easy, but it is not always so easy to determine the type of the disease. The endocarditic form in children, accompanied with great dilatation and hypertrophy, and often with other valvular lesions, presents no difficulty. Nor in adults, with the triple manifestations of a dislocated apex beat, a loud, rough, systolic murmur, and a greatly accentuated, pulmonic sound, is there any real difficulty. In the hypertrophied heart of chronic nephritis, in myocarditis from whatever cause, and in the relative insufficiency, it may be very difficult to determine whether there is an actual lesion of the valve, or not. Usually the murmur in these cases is less intense, and shows marked changes in varying the posture of the patient. It may be present in the recumbent, absent in the erect position, and it may disappear entirely as the general condition improves, or as the dilatation of the heart subsides.

Prognosis.—Among valvular lesions it is at once the worst and the best. The state of the myocardium is important. With the endocarditis of children, insufficiency may quickly reach a grade beyond the powers of compensation. On the other hand, a slowly induced insufficiency, combined with a moderate degree of narrowing may become stationary, the edges of the valves calcify, the heart hypertrophy is well maintained, and the patient may live a long and useful life without serious discomfort. It may be said that, as a rule, in children under ten the prognosis is bad more particularly as they are apt to have recurring attacks of rheumatic fever, and the condition is not so much a valvular lesion as a general carditis. The older the individual at the time of the onset of the endocarditis, the better is prospect. The arteriosclerotic variety may not diminish the expectation of life. Indeed the discovery of a mitral bruit, at examination for life insurance, may promote longevity. Warned to be cautious, the patient takes better care of himself and avoids, so far as possible, stress and strain. In the cases of relative insufficiency the prognosis depends much more on the condition with which it is associated than on the valvular leak.

STENOSIS OF THE MITRAL ORIFICE.

Etiology and Pathological Anatomy.—The disease is most frequent in females. Of 196 cases at Guy's Hospital collected by Samways, 107 were females. In the Edinburgh Hospital statistics of 1914 cases of valvular disease, 304 were mitral stenosis alone, 231 were mitral stenosis and insufficiency, and 26 were mitral stenosis with an aortic lesion. The stenosis is frequently not present alone, and insufficiency in some grade is a very common accompaniment. In fact, it may be said that the classical malady described as mitral insufficiency is almost always associated with some degree of stenosis; while mitral stenosis, except in a few rare instances, always permits of regurgitation. Etiologically, there are four groups of cases: (1) Those which follow an acute *endocarditis*. This is the most common form, and it occurs in the young and particularly in young

girls. Rheumatic fever is the dominant factor, and next to it chorea. Of 140 cases of chorea, examined more than two years subsequent to the attack, 72 had signs of organic disease of the heart, and 24 of these presented the physical signs of mitral stenosis. Scarlet fever, measles, and whooping cough may be responsible for a few cases. It has been claimed that tuberculosis plays a certain role, but for this there is not much evidence. As to the influence of mitral stenosis on pulmonary tuberculosis there is difference of opinion. The studies of Tileston¹ suggest that patients with mitral disease have a relative immunity to tuberculosis, and if it be present, the pulmonary disease is mild with a strong tendency to cure. (2) Those associated with congenital syphilis; some feature, such as Hutchinsonian teeth, deafness, interstitial keratitis or bossed skull, being invariably present; only a small proportion of cases give a positive Wassermann reaction. (3) In a small group of cases the stenosis is the result of a *primary sclerosis* of the valve with thickening and adhesion of the edges, shrinking of the chordæ tendineæ, with wide-spread atheromatous changes in the substance of the valve and in the mitral ring itself. It is not always easy to determine whether or not these changes have been initiated by an endocarditis, but this group occurs at the older period of life, and in men as well as in women. Newton Pitt pointed out the frequency of association with chronic interstitial nephritis, 33 cases in 542 autopsies. (4) Lastly, there is an important group of cases met with almost exclusively in women, in which *no positive factor* can be determined. The cases are usually latent, found accidentally, and the condition may persist for many years without causing any symptoms. In adult women, in whom this form is most common, one is almost always safe in putting the interrogative negatively--you have not had rheumatism. Some have thought that this form may be congenital, but this is unlikely, as it is rare to meet with lesions of the mitral valve during fetal life or immediately after birth.

A functional or spasmodic stenosis of the mitral is spoken of, due either to spasm of the sphincter muscle or of the papillary muscles. The cases have been described in hysterical patients, and in anemic and chlorotic subjects.

Anatomically, there are two forms, the pure or membranous, in which the left auriculo-ventricular ring is surrounded by a thin membrane representing the fused valve segments, perforated by a narrowed orifice which admits the tip of the little finger. The membrane is a little thickened, but it is pliable, the edges are smooth and may be readily placed in apposition, so that it is possible, during life, that the valve has been competent. These are the cases of what the French call *pure* mitral stenosis, and it is this form more particularly that is met with in women, in whom no history of any etiological factor can be found. From the auricle, this form presents a remarkable funnel shape. In the other variety, the valve segments are greatly deformed, the chordæ tendineæ thickened, and with the irregular calcified excrescences with atheromatous plates, the whole valve and ring are converted into a rigid mass, in

¹ *Jour. Am. Med. Assn.*, 1908, 50, 1179.

the middle of which there is a linear slit or a rigid orifice that admits the tip of the thumb or index finger. From clinical observations stenosis usually requires for its development at least five years from the initial attack of endocarditis. The heart itself is not greatly enlarged, and may not weigh more than 14 or 15 ounces. In elderly persons the organ may, indeed, look small. The left auricle, as a rule, is greatly enlarged, and may hold several hundred cubic centimeters of fluid. Normally, the capacity is under 50 cc. Cases have been reported in which it has held 500 or even 650 cc. The appendix is usually greatly enlarged. The endocardium is very opaque, and when the dilatation is extreme, the walls are very thin and fibrous. In the early stages, as Samways pointed out, the hypertrophy of the auricular walls is very marked.

The chambers on the right side are much enlarged, the ventricle contrasting in a remarkable way with its fellow; indeed, the apex of the heart may be made up entirely of the right ventricle. While this may be said to be the rule in mitral stenosis, there are some instances in which this contrast is not so striking, and the left ventricle may also be hypertrophied. The right auricle is greatly enlarged and the tricuspid orifice is much dilated.

Circulatory Adjustments.—Much of what has already been said of mitral regurgitation is true also of mitral stenosis. An increase of auricular pressure occurs at the end of diastole leading to stimulation and later to hypertrophy of the auricular muscles. Increase in auricular pressure, from further obstruction, causes such stretching of the muscle that increased action assisted by hypertrophy is not able to overcome the additional pressure. The orifices of the pulmonary veins now remain open during auricular systole, the pressure gradient in the pulmonary vessels becomes less steep and hypertrophy and increased action of the right ventricle follow as the result of the increased power required to empty the right ventricle. Mackenzie's view of the cause of the irregular pulse of mitral stenosis is now generally accepted. He noticed that when the crescendo murmur of mitral stenosis fails, or is replaced by a low-pitched murmur, the irregular pulse appears; moreover, at the same time, the evidence of the contraction of the left auricle fails. The condition is almost the invariable accompaniment of auricular fibrillation. The very rare persistence of the presystolic murmur has not been explained.

In mitral stenosis the left auriculo-ventricular orifice is narrowed, hence, unless the auricular muscle is particularly strong, the ventricle does not receive as much blood as it should normally. This is especially so in the severer forms of stenosis. There is, therefore, no tendency to a dilatation or hypertrophy of the walls; in fact, with less inflow into the ventricle, the cavity tends to become smaller and the bulk of the muscles less. In experimental stenosis, produced either by constriction of the auriculo-ventricular groove by a ligature, or by introducing into the auricle a distensible balloon, the pressure in the systemic arteries falls; that in the left auricles and pulmonary artery rises. The blood-pressure in man is not abnormally low; in fact, the same feature as has been noticed in mitral regurgitation may be present—namely, a very small pulse with a blood-pressure slightly above normal. With good compensation there

is but little departure from the normal, and when irregularity sets in, the maximum pressure varies considerably.

Symptoms.—*Latency* may be said to be the special feature of the lesion. At a busy clinic, not a month may pass without meeting the most typical physical signs in a person who has had no symptoms whatever. Extreme narrowing may be present, with nothing more than slight shortness of breath on exertion. In other instances, the patient for years has irregularity of the pulse and is short of breath on exertion. We must recognize a large group of cases in adults, in whom the lesion is well borne for an indefinite number of years. In children it is different, particularly in the cases that follow rheumatic fever. There is very often failure of development. They remain feeble, the breath is short, they are anemic, and there is a liability to fresh attacks of endocarditis. Many patients present for years a slight cyanosis, more particularly of the cheeks and of the ears, and are liable to have recurring attacks of bronchitis.

The symptoms of cardiac breakdown are very much the same as in other forms of valvular disease. The irregularity becomes more marked, œdema of the feet and ankles occurs, the breath is short and the signs of stasis are present in the viscera. Brisk hemoptysis may occur, sometimes with relief. Paralysis of the left recurrent laryngeal nerve may result from pressure of the enlarged left auricle. This, in connection with a wide area of impulse in the second, third, and fourth left interspaces, may lead to the diagnosis of aneurism. The senior writer saw two cases of this kind and others are reported.

Accidents in the disease are common, such as sudden attacks of congestion of the lungs and acute infarction with hemoptysis. Sudden death in acute cardiac failure may occur. Embolism is very common, the embolus being either a fragment of a clot from the dilated left auricle, or more frequently a fresh vegetation is whipped off from the orifice of the valve and plugs the left Sylvian artery, causing right hemiplegia and aphasia. In other instances there is embolism of the peripheral arteries. In rare cases, wide-spread thrombosis may occur.

Physical Signs.—**Inspection.**—Nothing may be noticed. The apex beat may be in the normal situation and the heart, indeed, may appear to be smaller than normal. In other cases, the apex beat is moved 1 or 2 inches to the left, the impulse is more forcible and there is marked pulsation in the parasternal line and in the lower sternum. In children, the precordia usually bulges, and there is marked pulsation in the interspaces along the left margin of the sternum, from the second to the fifth or sixth. In advanced cases, the pulsation of the enormously enlarged heart may be seen to the right of the sternum, but in pure mitral stenosis the hypertrophy of the heart rarely reaches the degree seen in insufficiency. When the left auricle is greatly dilated, pulsation may be seen in the first or second space to the right of the sternum where pain is also located.

Palpation.—In a considerable proportion of all cases, when the lesion is well compensated, the diagnosis may be made by palpation alone. At the apex is felt a purring thrill—limited in area, rarely felt above the fourth rib, most marked during expiration; occasionally only brought out after exertion. Coinciding with the diastole of the ventricle, it may

be felt throughout the whole period, or only in the latter part, rising crescendo-like toward the end and terminating in the sudden, sharp shock of the first sound. The localization, the occurrence in diastole, the purring, vibratory quality, and the abrupt termination in the first sound, form a quartet of signs that rarely lead us astray. As the disease advances and a stage of decompensation is reached, the thrill may disappear.

Percussion.—In the early stages there may be no increase in the area of cardiac dulness. With the increase of the left auricle, the dulness to the left may be increased, but the great enlargement is in the right ventricle, with extension of the dulness to the right of the sternum. The absolute cardiac flatness reaches high on account of the enlargement of the conus arteriosus. The great dilatation of the left auricle may compress the upper lobe of the lung, and the area of deep dulness may be much increased upward in the third and fourth interspaces. But the auricle itself rarely comes in contact with the chest wall. This enlargement of the auricle is well seen with the fluoroscope.

Auscultation.—In compensated cases, there is heard in diastole a rumbling, vibratory, or purring murmur, usually increasing in intensity and terminating abruptly in a loud, snapping, first sound, best heard over the apex with the patient lying on the left side. The special features of the murmur of mitral stenosis are: (1) Its *limitation*: the bell of the stethoscope may cover the region in which it is heard. (2) The *quality*: vibratory, grating, or a low, echoing rumble; with the exception of the rare instances of tricuspid stenosis, this quality of murmur is heard only at the mitral orifice. (3) The *sharp, valvular, first sound*: There are many modifications and changes. In the early stages there may be nothing more than a slight echoing rumble, and it is only on exertion that the characteristic murmur is brought out. Its position in diastole is variable. It may occupy the entire period, rising crescendo-like toward the close. It may be purely presystolic, occupying only the terminal portion and running directly up to the sharp valvular first sound. In other cases it is mid-diastolic, and the perceptible short interval separates it from the first sound. In this case it has to be carefully distinguished from the third sound of the heart which is frequently heard in normal persons, and especially under conditions of slight excitement. No other murmur may be present. A very soft systolic may be heard in some cases, with very slight extent of propagation. When decompensation is present, the typical presystolic murmur may disappear and a loud systolic is heard.

The state of the *sounds* of the heart in mitral stenosis is of exceptional interest. The shock of the first sound is extraordinary forcible. Except in certain neurotic states, no such snapping shock is felt at the apex. On auscultation, too, it is remarkably intense, and instead of a dull, thudding sound, it is of a flapping, even of an amphoric, ringing quality. So intense may it be that we meet here one of the few conditions in which the heart sounds are audible at a distance from the chest wall. It is common enough to hear the first sound a few inches away, but twice it has happened in the senior writer's experience to hear a clear, bell-like first sound when sitting at the bedside of the patient. In one case the distance was a little over 6 feet. Naturally, this loud, ringing sound is

propagated to the back. The second sound may be well heard at the apex, sharp and accentuated, increasing greatly in intensity as the stethoscope is passed toward the second left interspace. Here it is often reduplicated. In later stages the second sound may disappear at the apex, while it is loudly audible at the base. With the banking up of blood in the pulmonary system a dilatation of the pulmonary artery may appear with relative insufficiency of the pulmonary valves and a soft diastolic murmur (Graham Steell) in the second left interspace near the sternum.

In the stage of *decompensation*, with fibrillation, as Mackenzie first pointed out, the presystolic murmur disappears. Time and again the diagnosis of mitral stenosis is made for the clinician by the pathologist. A week's rest in bed with the use of digitalis may serve to bring back a presystolic murmur. In other instances a murmur of typical quality and a first sound of amphoric timbre may disappear and be replaced by a loud mitral systolic. An acute illness, a period of debility from any cause, may cause the murmur to become very feeble or even to disappear. In such instances there may be nothing but a faint diastolic rumble, which is changed into a more definite murmur on exertion.

The electrocardiogram in the stage before auricular fibrillation shows a marked *P*-wave in Lead II, a small *R*-wave in Lead I but large in Lead II and III, and an *S*-wave which is large in Lead I but small in Leads II and III.

In uncomplicated cases, no murmurs are heard at the aortic area. The first sound is usually very feeble in comparison with the second.

Diagnosis.—No valve lesion is more readily recognized than mitral stenosis, but in the earliest stage the murmur may be absent at rest though brought out by slight exertion or by amyl nitrite. One has always to bear in mind that when the terminal stage is reached, and the patients are admitted with fibrillation, the murmur is no longer present, and the diagnosis may be perhaps only suggested by the sex of the patient and by the fact that there is a somewhat snapping first sound. A murmur with the same quality during diastole at the apex, is heard in aortic insufficiency, known as the Flint murmur, and has been discussed. The Graham Steell murmur of pulmonary insufficiency is often mistaken for aortic insufficiency; the absence of signs of aortic regurgitation in the pulse and the dilatation of the pulmonary artery on the roentgen-ray screen may be used to distinguish the two conditions. In tricuspid stenosis a rumbling presystolic murmur is heard, of maximum intensity over the body of the heart. In the conditions in which the senior writer has heard it, mitral stenosis has always been present as well. And lastly, in a considerable number of cases of pericardial adhesions, a rumbling apical murmur is heard in diastole. It rarely has the peculiar limited localization, nor does it end in a snapping first sound.

Prognosis. Mitral stenosis is a serious lesion and exceedingly so in children. The rheumatic form being so frequently progressive is the gravest form. The average age at death from the published figures of several observers is thirty-five years. Isolated patients may occasionally be seen aged fifty or more years. Incidental infections, especially bronchial, interfere with health as life progresses.

Treatment.—Considerable benefit has been reported by Cutter and Levine¹ who performed valvulotomy on a patient aged twelve years.

TRICUSPID INSUFFICIENCY.

Etiology.—There are two groups of cases, one the result of organic disease of the valve cusps, the other relative or functional incompetence from dilatation of the tricuspid ring due to lack of tone (muscular insufficiency) in the right ventricle.

1. *Organic disease* follows rupture, endocarditis, or a chronic fibrosis of the segments. (a) Rupture of the valves or of the chordæ tendineæ may follow a blow on the chest or an excessive effort. (b) The endocarditic form occurs in the acute infections, more particularly rheumatic fever. (c) The etiology and appearance of fibrosis of the tricuspid valves are similar to those of the mitral.

Because of the lessened strain put upon the tricuspid valve in adult life, inflammation and degeneration of its leaflets are much less frequent than in the mitral valve. Probably also because of the greater tension during fetal life, the relative frequency of endocarditis in the right and left side is reversed. Congenital endocarditis is almost always confined to the right side of the heart. In adult life affections of the tricuspid are rare. By far the most frequent cause is rheumatic fever, and when present on the right side, endocarditis is, in the majority of cases, associated with the same process of the mitral valve, of the aortic valve, or of both. In addition, affections of the valve have been determined to be due to various organisms. Gummatous change of the valves has been described. As a sequence of other valvular disease, mitral or aortic, degenerative changes may cause insufficiency. Malignant disease is extremely rare.

2. *Relative insufficiency* arises in a large number of conditions. The fibrous ring which surrounds and supports the auriculo-ventricular orifice is liable to become stretched, and at the same time the muscle of the ventricle suffers distention. This means a larger orifice for the valves to close, and as the chordæ tendineæ cannot elongate, the orifice remains open, its cusps not being able to meet in close apposition. It is a question whether the inability of the muscle to lessen the ventricular cavity to its normal size in systole does not play a large if not the chief part, for if at the height of systole the cavity were no larger, it is conceivable that, even with a dilated ring, no regurgitation might occur; but if with a dilated ventricle, the degree to which the ventricle can contract be lessened, then the cavity is fuller at the end of systolic than normal, and the valve cusps are not properly approximated.

The important part played by the muscle of the ventricle was put forward in a masterly way by T. Wilkinson King² in 1837, and the account which he gives of the anatomical relations of the tricuspid valve and its connection needs no revision. "The right auriculo-ventric-

¹ *Boston Med. and Surg. Jour.*, 1923, 188, 1023.

² Safety Valve Action in the Right Ventricle of the Human Heart, *Guy's Hospital Reports*, London, 1837, 2, 104.

ular opening is oval; and to its circumference, the membrane of the tricuspid valve has attachment, without any distinct interruption; while its floating border, depending into the ventricle, is deeply fissured, so as to form three or more scalloped or angular curtains. And it appears from careful examination that the united areas of these valvular portions are scarcely more than equal to the mean extent of the oval opening. One of these curtains (which, not being movable, I have called fixed) occupies the left margin of the aperture in apposition with the solid wall, from which arise all the cords that serve to secure the free edges and ventricular surface of the fixed curtain. These cords are of such a length as scarcely to allow the curtain to rise into the plane of the oval opening in the natural play of the valve, and being destitute of muscular columns, cannot by any possibility set the valve in motion, or serve any other purpose than that of preventing too great a reflex of the curtain itself. A second curtain (the anterior) is attached at the anterior and right edge of the opening, having one free border forward and another backward in the ventricle. Each border has its proper set of cords: the anterior, or upper, set having their insertion into a mere nipple of muscle on the solid wall, in the direction of the pulmonary artery; and the inferior, or posterior, are as invariably collected with numerous others into the summit of a muscular column, whose base is inserted into the thin right, or yielding wall, of the ventricle near its centre, where also is attached, almost as regularly, another muscular band which stretches across the cavity between the two walls. This band may have an average length of six or seven lines and a circumference of three or four. It seems calculated to limit distention, and therefore I have called it the moderator band of distention. The third curtain or fold of the valve (the right) is situated on the right side of the aperture posteriorly, and has little or no connection with the inner or left edge of the opening. In extent and figure it varies considerably, and it rarely forms one single scallop, but is frequently fissured so as to form two or three, more or less complete. Its cords are accordingly arranged in two or more sets, the greater part of which are attached by the intervention of muscular columns to the outer yielding wall, at a considerable distance from the solid wall, and usually without any transverse bridge or moderator band.

"The construction . . . I have described in connection with the yielding, *i. e.*, the outer wall of the ventricle, constitutes the main peculiarity of arrangement and action in the tricuspid valve, the great extent, thinness, and feebleness of the yielding wall rendering it liable to the distending influence of venous accumulation in various degrees; the curtains being three, and each one tethered to that part of the ventricular parietes immediately beneath itself (but most extensively to the yielding wall), by the intervention of columns whose passive effect is to produce a retraction of the curtains in proportion to the distention, and whose active contractions serve, under dilatation, to augment the valvular retraction, or rather to maintain it at its height during the imperfect systole . . . and further, the orifice itself, depending on the yielding wall, may admit of some relaxation and thus assist to produce regurgitation."

Following these anatomical observations, King performed several experiments on human hearts in which no disease could be detected. By putting pressure into the left ventricle, it was easy to effect a complete and adequate closure of the mitral valve, and only with very considerable pressure did the escape of water into the auricle occur. In the right ventricle, however, no position of the heart and no variation of the conditions were sufficient to prevent the escape of a tape-like stream of water into the right auricle, unless the walls of the ventricle were at the same time compressed by the hand. King suggested the effect of cardiac tonicity on the production of a complete valvular ring, and demonstrated it by showing in a heart, in which rigor mortis appeared after removal, that the deficiency of the valve became almost negligible.

Relative tricuspid insufficiency, therefore, is caused by affections interfering with the muscle of the right ventricle, and its causes may be summarized as follows:

(a) *Mechanical dilatation*, due to an increase in pressure in the ventricle at the beginning of systole, may be caused by overexertion, asphyxia, and abnormal fixation of the chest wall, as in some forms of labor. Other causes oppose obstruction in the pulmonary circulation—chronic bronchitis, sclerosis of the lung arteries, bronchiectasis, chronic fibroid disease of the lungs and pleura, and disease of the mitral valve. The ease with which this dilatation is brought about may be shown by the fact that, by holding the breath for one minute, the right border of the heart moves to the right at least an inch.

(b) Dilatation of the right ventricle, the result of a failure in muscular nutrition, is observed in all forms of local cardiac disease, myocarditis, pericarditis, etc. Of general diseases, the most important are malnutrition, as in diabetes, cachexia, debility and in the anemias, especially in pernicious anemia. Prolonged and high fever tends to an enfeeblement of the cardiac muscle and to insufficiency of the tricuspid valve.

Circulatory Adjustments.—*Mutatis mutandis*, what has been said of mitral regurgitation applies here. With insufficiency, the first stress is thrown upon the right auricle, which, by hypertrophy and compensatory dilatation, opposes a mechanism against the effects of regurgitation. When the regurgitation becomes greater and the cavity of the auricle has to dilate to such an extent that it cannot exert sufficient force on the contained blood, the muscle bands by which the orifices of the veins are closed during systole are stretched and become ineffective. There is then during systole of the ventricle, a continuous column of liquid from the ventricle into the veins without the opposition of any valvular mechanism. It is obvious, then, that the condition of the venous system, from the clinical aspect, is of considerable importance. Mackenzie showed by tracings that when the right side of the heart is at fault, as in failure from mitral disease, a change often comes over the jugular pulse in which the auricular wave diminishes or disappears, and the ventricular wave increases in size and occurs earlier in relation to the ventricular output, than in normal cases.

The transition is shown diagrammatically in Fig. 38. When the alteration is fully developed, there is only one large wave in the jugular pulse,

which for the most part is ventricular in time. Mackenzie called this form of venous pulse the "ventricular" form, and took it to mean tricuspid regurgitation. This view has received confirmation by Rihl,¹ who, by making an artificial lesion of the tricuspid valves in rabbits, finds that, according to the severity of the lesion, there are two sharply defined forms: first, that in which the regurgitation is slight and the venous pulse shows no change from the normal; and, secondly, that in which the venous pulse is of the ventricular form. We must suppose that in the former condition, the auricle of itself can compensate for the regurgitation, without undue stretching of its walls by the regurgitated blood. This is confirmed by finding that in these less severe forms, stimulation of the vagus, the beginning of asphyxia, and so on, which in the normal animal are without effect on the jugular pulse, in the mutilated animal, produce a ventricular venous pulse.

Morbid Anatomy.—The heart in pure tricuspid insufficiency has certain distinctive features. The right auricle is dilated and globular, the right ventricle is more prominent and fuller than normal, and appears to be creeping round the left ventricle. The amount of distention of the right auricle and ventricle depends on the rapidity of onset of the lesion, on whether organic disease is present in the valves, the condition of the muscular walls, and so on. The best example of a pure functional tricuspid insufficiency is to be seen in death from asphyxia, in which the right heart, especially the auricle, is enormously dilated. When organic disease of the valve is present, the ventricle and auricle have had time in part to oppose a certain amount of hypertrophy against the valvular defect, consequently in the organic cases the enlargement is not so great, and is made up of hypertrophied muscular wall, in addition to the dilated cavity.

The condition of the valve in relative or functional insufficiency is normal, the cusps being thin and the chordæ tendinæ not thickened or shortened. In the case of organic insufficiency, the state of the valve will vary according to the cause. A recent endocarditis takes the form of

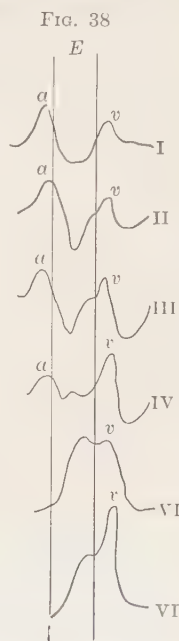


Diagram to show the transition from the normal venous pulse to the ventricular pulse, i. e., in tricuspid insufficiency. *I*, is the normal venous pulse from which the *c* wave, occurring between *a* and *r*, probably due to the carotid artery, has been omitted; *a*, auricular wave; *v*, ventricular wave, whose significance in the normal venous pulse is doubtful. *E*, period of outflow into the pulmonary artery. (After Mackenzie.)

¹ *Verhandlungen des Congresses f. innere Medizin, Wiesbaden, 1907 Band XXIV.*

small excrescences, or larger irregular masses, attached to the valves. If, on the other hand, there is chronic fibrosis, the cusps are thickened, glistening white or yellowish, and the chordæ tendineæ thickened and shortened. The mural endocardium in the chronically dilated cavity is always thicker than normal. On account of the pressure to which they have been subjected, the veins opening into the right auricle are dilated, their walls are slightly thicker than normal, and this thickening extends into the jugular and the subhepatic veins.

The liver, spleen, and kidneys all show the chronic cardiac congestion described under mitral disease; in fact, these appearances in the two diseases are due to failure of the right side of the heart. The lungs in experimental animals are dry and bloodless, and the same has been noted in pure cases of tricuspid insufficiency in man.

Symptoms.—The chief complaint of the patient is breathlessness on exertion, and if the lesion is uncompensated, there is quickened breathing or orthopnoea, even at rest. The slightest exertion causes dyspnoea and a sudden sense of oppression in the chest. In advanced cases orthopnoea is marked. Pain is not a prominent symptom. It most frequently occurs in relation with an enlarged liver whose capsule is stretched, and consequently the pain is felt on the right side of the abdomen. The digestion is always faulty and the appetite is lessened or absent. Distention of the abdomen, either in relation to meals or not, is common, relieved sometimes by eructations or by purgatives. Œdema of the legs and feet sets in early and is of the usual type, being less evident after a night's rest in bed. Ascites may be present even before any œdema occurs.

Physical Signs.—The facies of the patient with marked regurgitation is one of intense *cyanosis*. The whole surface of the skin is a livid blue color, the extremities, such as the ears, the tip of the nose, and the fingers being of a deeper color than the rest of the skin. The lips are a violet blue. The sclerotics are darker than normal and of a subicteric tint. The visible veins, such as those of the temple, neck, arms, and chest, are dilated and prominent. If noticed carefully, two types of pulsation may be distinguished in those of the neck: first, rhythmical emptying and filling; secondly, pulsations synchronous with the heart beats, best seen in the right supraclavicular triangle outside the sternocleidomastoid, over the spot where the external and internal jugular veins enter into the subclavian. In fact, the jugular sinus may be so dilated as to form a rounded swelling just above the clavicle. The pulsations may extend over the veins of the shoulders and mammary regions and down the superficial veins of the arm and the elbow. Inspection may show a large area of precordial pulsation, especially noticed over the lower end of the sternum and in the epigastrium. In cases with a marked pulsation in the jugular veins, pulsation in the liver can usually be both felt and mechanically recorded.

The apex beat is diffuse and extends outward to the left as far as the nipple line or farther into the left axilla. On palpation, sometimes a light systolic shock may be perceived. On determining the limits of pulsation, the area is found to lie over the lower end of the sternum and along a strip stretching from the sternum to the apex beat, an area corre-

sponding to the right ventricle. On percussion, the transverse dulness is increased and stretches more to the right than normal.

On auscultation a *systolic murmur* can usually be detected in the cardiac area. It may be rough, especially if the insufficiency is the result of endocarditis. On the other hand, if the insufficiency is relative, it is faint and delicate. Tricuspid systolic murmurs are more superficial than mitral; their pitch is higher and their duration longer. Tricuspid murmurs are accentuated if the patient is lying flat on his back with the head strongly extended backward. The point of maximum intensity is over the sternum and to the left rather than to the right. It may, however, be heard to the right of the sternum, which can hardly ever be done in mitral insufficiency. The roentgen-rays may be used as a means of distinguishing this condition. In a case of pure tricuspid insufficiency, the maximum pulsation is toward the right border of the heart, and the extended pulsation of the left auricular region, so characteristic of mitral failure, is absent.

Diagnosis.—From a careful observation of the jugular pulsation in the neck, and careful auscultation over the precordia, there is seldom much doubt as to the presence or absence of tricuspid regurgitation. The veins of the neck show, in proportion to the deficiency of the valve, a pulsation which is synchronous with the ventricular systole. If, by observation, the time of the most prominent wave is not easy to determine, then a tracing, especially combined with an apex tracing, will determine exactly the time of the jugular pulsation. To distinguish the murmur of mitral regurgitation from that of tricuspid regurgitation is by no means always easy. Mitral systolic murmurs may be loudest at almost any point to the left of the sternal border, below the second interspace; less frequently they have their maximum intensity over the ensiform process. The tricuspid murmurs are soft, blowing, rarely rough, more superficial, shorter, and usually higher in pitch. The loudest can be heard over the entire sternal area, generally plainest opposite the fourth interspace, and more distinct over the middle and left half than toward the right side of the sternum. Less frequently they are heard best over the lower half of the sternum. The conduction of the murmur may be either to the right or to the left, to the left better than to the right. Faint murmurs are not heard above the third rib.

It is important to determine whether the incompetence is relative, due to stretching, or from organic change in the valves. The following points are suggested by Schwartz:¹ With a positive venous pulse and a percussion dulness of the right border of the heart not extending beyond three fingers' breadth to the right of the right sternal edge, an organic lesion of the tricuspid is the more probable. If, on the other hand, the right cardiac dulness extends farther to the right than three fingers' breadth, a relative insufficiency is more probable, because the valves are insufficient by the stretching of the muscle, which may be so great as to make the right border extend by percussion to the right mammillary line. In organic insufficiency after the reestablishment of compensation,

¹ *Verein f. innere Medizin*, Abstract in *Deutsch. med. Wchnschr.*, 1903, 5, 318.

the positive venous pulse remains, while in relative insufficiency, the positive venous pulse is replaced by one in which the auricular wave becomes more prominent.

Prognosis.—In those cases in which the deficiency is due to organic disease, the prognosis is always grave, for only very rarely is it unaccompanied by disease elsewhere in the heart and because any failure of the right ventricle is immediately followed by symptoms of heart failure. In relative tricuspid insufficiency, the prognosis depends more on that of the cause of the insufficiency than on the valvular defect itself.

TRICUSPID STENOSIS.

Etiology.—Tricuspid stenosis may follow an infective process or be the result of a primary degeneration of the tissue. The character of the infection is often doubtful. Leudet, in 1888, collected a series of 114 cases. Herrick, in 1897, added 40 cases. Newton Pitt, in 1899, collected from the records of Guy's Hospital a total of 87 cases out of 12,000 post-mortem examinations, and Wardrop Griffith, in 1903, studied 19 cases from the postmortem records of the Leeds Infirmary and the specimens in Yorkshire College Museum. In a majority of cases, rheumatic fever was the most important single factor. In the 173 cases of Leudet, Herrick, and Griffith, 59 had a definite history of rheumatism or chorea, *i. e.*, 34.9 per cent. In Newton Pitt's series, the percentage is much greater, 62.06 per cent.; and if the cases with a history of vague rheumatic pains be admitted, the proportion becomes somewhat larger. Of other infections causing tricuspid stenosis we have no certain knowledge. Syphilis is mentioned as an antecedent in one of Griffith's cases. Two cases have been reported in which a pedunculated ball-like tumor projected down from the auricle and partially occluded the tricuspid valve. A hernia of the undefended space and a knob-like bulging into the right side was the cause in a case observed by the junior writer.

Females are affected much more frequently than males; in a total of 260 cases collected by Leudet, Herrick, Pitt, and Griffith, 179 were females, 63 were males, and in 15 the sex was not mentioned. The age incidence at death is well shown from Pitt's series of cases: between eleven and twenty years, 16 cases; between twenty-one and thirty years, 31 cases; between thirty-one and forty years, 22 cases; between forty-one and fifty years, 10 cases; between fifty-one and sixty years, 3 cases; between sixty-one and seventy years, 2 cases.

The association of other cardiac lesions is a special feature in tricuspid stenosis; thus, in the 173 cases collected by Leudet, Herrick, and Griffith, the following valvular lesions were found: stenosis of the tricuspid valve alone in 12 cases; stenosis of the tricuspid valve with mitral stenosis in 97 cases; with pulmonary stenosis in 3 cases, with lesions of the aortic and mitral valves in 58 cases, and with lesions of the mitral and pulmonary valves in 3 cases.

Circulatory Adjustments.—A pure stenosis, gradually increasing in degree, causes an overfilling of the right auricle, and by stretching the muscle of the auricular wall, this leads to more vigorous contractions

and is followed by hypertrophy of its muscular wall. As the stenosis increases, the auricle, even although hypertrophied, will not be able to empty its contents during systole, and consequently the cavity enlarges. The closure of the veins which open into the right auricle is probably effected by the muscular bands, especially those which lie around the venous openings. In the dilated auricle these are unable to contract properly and the veins remain open. Consequently, at each auricular systole a regurgitant wave, presystolic in time, travels up and distends the vein. The hypertrophy causes a greater wave than normal. With increase in the stenosis, the auricle tends to become so dilated that its power, even although hypertrophied, is inadequate to expel more than a fraction of the blood into the ventricle. The auricular pulsation then fails, and with it the transmitted pulsation in the jugular veins. These two conditions correspond to two types observed clinically: first, the cases in which there is jugular pulsation in turgid veins, auricular in time; secondly, the cases in which, although the veins are turgid, no pulsation can be observed in them.

Morbid Anatomy.—The general appearance of the body is the same as that in death from chronic mitral disease with anasarca. The cyanotic tint is more marked than in other cardiac lesions. As tricuspid stenosis is so often associated with mitral stenosis, it is not always easy to say which anatomical features correspond purely to the former. The chief feature is a marked enlargement of the right auricle associated with a dilatation and a thickening of the walls of the superior vena cava and its branches. This dilatation may be sufficient to do away completely with the function of the valves, so that there is a continuous cavity from the venous system to the right auricle. This is well shown in one recorded case in which there was a continuous clot extending from the right auricle into the veins of the neck. The state of the right auricle depends upon the conditions of the circulation at the time of death; if this has occurred while the auricle by hypertrophic increase has been capable of propelling blood through the constricted orifice, the cavity of the auricle is large and its walls thickened by more layers of muscle fibres. But if the patient has lived a stage farther, the cavity is dilated and the wall of the auricle very much thinned, so much so, that in areas as much as 5 cm. across, the auricular wall is composed of epicardium and endocardium alone. The rest of the muscular tissue of the auricle is proportionately thinned in these cases. The endocardium of the auricle, in consequence of continued back pressure, undergoes increasing thickening, and at death is much less transparent than in a normal right auricle. The tricuspid orifice is narrowed in different cases, to different degrees; cases have been reported in which it scarcely admitted the little finger. The three cusps are so welded together and thickened that they are indistinguishable, except by comparison with their relations to the papillary muscles. The chordæ tendinæ are thickened and shortened. Other appearances have been described. In the case reported by Gairdner the orifice was blocked by a fibrinous ball attached to a point on the auricular wall. In another case reported by Philip,¹ large recent vegetations filled up the cavity. The

¹ *Edinburgh Hosp. Rep.*, 1893, 1, 235.

right ventricle showed some enlargement of its cavity and thickening of its walls. In almost all accurately recorded cases some degree of mitral stenosis has been present.

The condition of the lungs varies, and in this regard also we cannot distinguish the effects of a tricuspid stenosis from those of a mitral stenosis. They are sometimes found to be dry on section, with only a small amount of hypostatic congestion at the bases and no marked œdema, sometimes markedly œdematous and congested with pneumonic consolidation at the bases, or with hemorrhagic infarcts. The liver, although presenting the appearance of chronic stasis, is not always enlarged; in fact, some livers have been distinctly below the average size (Stow's case). The edges are rounded; the capsule is thickened, and, on section, the organ drips with very dark blood, showing a surface with the features of the "nutmeg" liver. A notable feature is the increase in connective tissue. Perihepatitis has been observed.

Symptoms.—That a considerable degree of stenosis may not be productive of symptoms is shown by the history, reported by Gairdner, of a man who was under observation for ten years, led an active life, and died at the end of the period from pneumonia. The symptoms of tricuspid stenosis are in the main very similar to those of tricuspid insufficiency, but they present certain important differences. Cyanosis may be present for a year, or even longer, before any other sign of cardiac failure. It is not of a very pronounced grade, nor so marked as that seen in extreme degrees of congenital heart disease, but is often sufficient to give trouble to the patient and to give occasion to remarks. Breathlessness is the most frequent complaint; it is more marked and comes on sooner than in lesions of the left side of the heart. Even very slight exertion, such as walking, may bring on severe dyspnœa. Other symptoms of heart failure differ in no respect from those in left-sided lesions, such as œdema, ascites, pain in the right hypochondrium from the engorged liver, indigestion, constipation, and so forth. In certain cases anginal pain is complained of, which may pass down the left arm, occasionally down the right. It is often questionable in a given case which symptoms are due to the tricuspid stenosis and which to the frequently associated mitral stenosis. Gairdner's patient complained of the jugular pulsation in the neck. All patients in whom the cyanosis is marked, complain of great susceptibility to cold. Hemoptysis, noticed in twenty cases in Newton Pitt's series, is probably due to the mitral stenosis.

Physical Signs.—**Inspection.**—The patient, as a rule, is cyanotic, the tint being most marked in the lips, nose, ears, and hands. The veins are dilated and may be specially noticed in the lower part of the neck. The jugular bulb may be dilated to such an extent as to produce an ovoid swelling, which may or may not show pulsation. If none is visible, it may often be brought out by getting the patient to sit or stand up. An important distinction between stenosis and insufficiency of the tricuspid valve lies in the form of the *jugular pulsation*; in the latter, the type of the jugular pulse is ventricular, *i. e.*, the most prominent wave is systolic in time; in tricuspid stenosis the largest wave is the auricular, and hence presystolic. Mackenzie pointed out this distinction and that the liver

pulsation, which is a constant feature of these cases, shows a large wave, also auricular in time. The narrowing of the tricuspid orifice protects the auricle from the overdistention due to a large regurgitant stream, while the overfilling of the chamber, from a diminished outflow through the contracted orifice, serves to stimulate the auricular muscle to vigorous action and hypertrophy. The auricular pressure forced into the veins in systole often causes so great a tension in the valves at the entrance of the internal jugular vein that an audible sound, auricular in time, is heard on auscultation over this area. When fulness without any pulsation is present, there is probably a paralysis of the right auricle from overdistention.

As, almost without exception, there is associated mitral stenosis, it is difficult to separate the signs due to tricuspid stenosis alone. The area of pulsation is greater than normal, the apex is usually localized with difficulty and is seen farther out to the left. Some pulsation is seen in the costo-sternal angle.

Palpation.—A thrill presystolic, sometimes systolic, in time can be felt, the presystolic having its maximum intensity over the lower end of the sternum.

Percussion.—The cardiac dulness is increased to the right and occasionally in the upward direction.

Auscultation.—In the majority of cases recorded there has been a rough presystolic murmur, not quite so harsh as that heard in mitral stenosis. The point of maximum intensity and its area of audibility differ in different cases, but it may be said generally that the maximum point is somewhere near the lower half of the sternum, and it is propagated radially from that point. Sometimes it is heard over the entire sternum, more distinctly to the left side, sometimes over the lower half of the bone. Occasionally the murmur is heard to the right.

Polycythemia is almost constant, and, as a rule, well marked, often 8,000,000 or 9,000,000 red cells per cubic millimeter. The fingers are frequently clubbed. If there is any cardiac failure, the urine contains albumin, and glycosuria has on rare occasions been noticed.

Diagnosis.—The reports of a large number of cases show that tricuspid stenosis may be mistaken for mitral stenosis, for tricuspid insufficiency, for congenital cyanosis, for pulmonary stenosis or deficiency of the septum of the auricles.

Considering the similarity of the symptoms in mitral and tricuspid stenosis, it is not surprising that the rarer lesion is occasionally overlooked. The points of distinction are as follows: The *cyanosis* in tricuspid stenosis is more marked and more constant; in mitral stenosis the cyanosis is more clearly associated with a loss of compensation and with pulmonary stasis. If digitalis be given to a patient with mitral stenosis, the cyanosis, as a rule, lessens, but in a patient with tricuspid stenosis little, if any, effect can be noticed. Attention should be paid to the following points: If the veins of the neck are full and pulsate with each auricular beat, tricuspid stenosis is more likely. In mitral stenosis with cardiac failure, insufficiency of the tricuspid would be produced and a positive, *i. e.*, systolic or ventricular, venous pulsation would be pro-

duced. The precordia should be carefully palpated to determine the area of any thrill that may be present. A presystolic thrill in the neighborhood of the apex suggests a mitral lesion; one more to the right, especially if its point of maximum intensity be felt on or near the sternum, suggests tricuspid stenosis. Careful auscultation sometimes shows that a presystolic murmur at the apex alters its character on being traced to the right, toward the sternum, and with its altered character becomes more intense in that region.

Several cases are on record in which physicians of great experience have mistaken a tricuspid stenosis for insufficiency, although repeated examination had been made for signs of tricuspid stenosis. Mitral stenosis with loss of compensation may be difficult to recognize and this is also probably true of tricuspid stenosis. The mitral stenosis, in the stage of loss of compensation, is mistaken for mitral regurgitation; similarly the tricuspid stenosis, with loss of compensation, is mistaken for tricuspid regurgitation. It is suggested that in those cases in which competent observers have diagnosed tricuspid regurgitation, the symptoms of stenosis had disappeared by the failure of the auricular contractions.

Prognosis.—The gravity of stenosis of the tricuspid valve depends on its association with mitral stenosis in a great number of cases. Mackenzie supposed that tricuspid stenosis protects the rest of the heart from the effects of overfilling. This view is borne out by Gairdner's patient, who led the life of a laborer for many years without any obvious symptoms. When mitral stenosis is present at the same time, the additional lesion means a much greater strain on the cardiac mechanism, and the length of life in such cases would be in proportion to the gravity of the lesion on the left side of the heart. In Newton Pitt's series of 87 cases, 31 died between twenty and thirty years of age, the others in a lessening proportion in the previous and succeeding age decades.

PULMONARY INSUFFICIENCY.

From the clinical stand-point, so much that has been said about pulmonary regurgitation is unproved or as yet incapable of proof that the subject should be approached with the greatest caution, and with as clear as possible a conception of the theoretical aspects.

Structurally, the pulmonary valve and its surroundings differ from the aortic valve in their more delicate texture, and in the adult the segments do not, as a rule, show the medial thickening about the corpora Arantii. The wall of the pulmonary artery is thinner than that of the aorta and has not the same tendency to preserve its ring structure in the absence of an internal pressure. The conus arteriosus which leads into the pulmonary is more thin-walled than the corresponding part of the left ventricle, and under increased internal pressure is probably capable of considerable dilatation. The structures in relation to the pulmonary valve are obviously directed to withstanding much less pressure than the corresponding parts of the aorta, and this is borne out by what is known regarding the relative pressures in the two sides of the heart.

G. A. Gibson showed that in the pulmonary artery of the sheep, pressures above $14\frac{1}{2}$ inches caused a strong jet of water to escape through the pulmonary valve into the ventricle; with less than this, and down to a pressure of 9 inches of water, there was a small escape; below 9 inches the valves were competent. In the healthy human heart much fluid escaped with a pressure above 13 inches, a small amount between 13 and 8 inches, and none below that pressure. We have no direct means of estimating the pressure in man. The results of animal experiments give as the mean pressure 17.6 mm. of mercury in the cat, 12.07 mm. in the rabbit, and 29.6 mm. in the dog (Bentner). Eight inches of water is equal to about 15 mm. of mercury, so that the pressure in the pulmonary artery in man at the height of a vigorous systole of the right ventricle may cause a pressure well above that which first begins to cause insufficiency.

Etiology.—Insufficiency of the pulmonary valve may be caused by an acute endocarditis, by chronic fibrosis of the segments, or by dilatation of the orifice. Insufficiency from acute endocarditis is seen in gonorrhoea, rheumatic fever, pneumonia, scarlet fever, pyemia, and puerperal fever. It is remarkable that in the cases collected by Newton Pitt, from Guy's Hospital, nearly one-half of those in which a definite infective cause was ascertained were due to the gonococcus. An interesting form is associated with aneurism of the aorta (Newton Pitt), in which an inflammatory change in the neighborhood extends to the pulmonary artery and causes an adhesion of one or more cusps of the pulmonary valve to it. Sclerosis of the leaflets is met with in long-standing cases of mitral disease, sometimes in emphysema and chronic affection of the lungs. Rupture and deficiency in the number of the valves are rare causes of insufficiency.

Relative pulmonary insufficiency may follow long-standing obstruction in the pulmonary circulation. Our knowledge of these conditions is very scanty, but those which are most certain are left-sided valvular disease, especially mitral stenosis (Graham Steell), and general pleuritic adhesions (Rokitansky).

Morbid Anatomy.—In certain cases of infective endocarditis the orifice of the pulmonary artery may be narrowed by the vegetations. The right ventricle is enlarged to a degree depending on the duration of the insufficiency. The pulmonary artery may show patches of atheroma, especially if the insufficiency has been due to an obstruction in the pulmonary circulation, as, for instance, in mitral stenosis. It by no means follows that with evidence of pulmonary regurgitation during life this can be demonstrated postmortem; it depends wholly upon whether the elastic tissue of the base of the pulmonary aorta has been damaged. The ordinary methods of testing the efficiency of the valve postmortem, namely, by pouring water into the artery in the excised heart or measuring the diameter of the pulmonary orifice, only give the efficiency in the collapsed state of the organ, and not when it is distended by blood. This is probably the reason why, in mitral stenosis, it is often possible to detect a diastolic murmur down the left of the sternum and yet seldom is it possible to find evidence of regurgitation postmortem.

Symptoms.—Only when failure of the right ventricle is present, do symptoms appear, cyanosis, dyspnœa, œdema, failure of appetite, etc. Epistaxis has been recorded in some of the cases, and in one case (Oliver's, 1907) it caused death. Hemoptysis from emboli in the lungs is frequent in infective cases. A third group of cases are those in which the signs of an infective process, such as puerperal septicemia, are the most noticeable, and, unless special attention be directed to the heart, are frequently not diagnosed during life.

Physical Signs.—The precordial area of pulsation is enlarged, the apex beat is to the left of the nipple line, diffuse epigastric pulsation is visible, and frequently pulsation to the left of the sternum in the second and third interspaces and jugular pulsation are present. The cardiac dulness is increased transversely. The auscultatory signs are the most important and those upon which alone a diagnosis can be made. The murmur of pulmonary regurgitation, as a rule, is coarser than that in aortic regurgitation, often grating, and more superficial. It is heard best down the left side of the sternum, and is propagated not along the systemic arteries, but along the left pulmonary artery. The second sound at the aortic area can usually be well heard, somewhat higher in pitch than that at the pulmonary valve, if present. It is often possible to detect pulsation in the lung vessels from the rhythmic constriction of the pulmonary alveoli; the vesicular murmur is rendered louder during ventricular systole.

Diagnosis.—This is at all times difficult; the following points require special attention: (a) The character and situation of the murmur, its presence down the left side of the sternum and the rougher quality than that produced at the aortic valve. (b) The character of the pulse; Corrigan's pulse being invariably absent in pulmonary artery disease, though it should be remembered that Corrigan's pulse is not invariably present in aortic regurgitation. (c) The murmur of pulmonary regurgitation is increased in intensity during expiration or in expiration with a closed glottis (Valsalva's experiment). (d) The apex beat in right-sided valvular disease is diffuse and displaced downward and outward.

Prognosis.—In the acute cases, the outlook depends on the cause of the endocarditis. The streptococcus, gonococcus, and pneumococcus cases are usually fatal. In the more chronic forms, some time is allowed for hypertrophy of the right ventricle, and not until this fails will there be signs of circulatory insufficiency. In relative insufficiency also a line of defence is present in the hypertrophy of the right ventricle; but the prognosis is associated rather with the original cause of the disease than with the pulmonary regurgitation.

PULMONARY STENOSIS.

This is an exceedingly rare, acquired lesion. The congenital form is discussed elsewhere, and only the acquired form is considered here.

■ **Etiology.**—The causes are much the same as in aortic stenosis. (a) Endocarditis is the most common cause, and may occur in rheumatic fever or one of the other acute infections. In some instances the vegeta-

tions are very large. (b) Chronic sclerotic changes may occur as at the aortic orifice, sometimes associated with endarteritis of the pulmonary artery. (c) Rare instances due to trauma have been recorded.

Morbid Anatomy.—The changes are much like those at the aortic orifice. In the form with endocarditis, the vegetations may be very large, and almost block the orifice. In some cases the process may be more in the conus arteriosus, and this is often due to endocarditis of the ventricular wall. In the sclerotic form the cusps are thickened, and may be adherent, forming a much narrowed orifice. Calcareous deposits may form, so that the orifice is nothing but a rigid ring, in which case the stenosis is accompanied by regurgitation.

Circulatory Adjustments.—Practically the same changes arise, as are found in the left heart in aortic stenosis. In pure stenosis, hypertrophy of the right ventricle is the most marked early change, as by this compensation is maintained; but, when insufficiency is combined, dilatation and hypertrophy result. With marked stenosis there must be some decrease in the pulmonary circulation. As the right ventricle fails, tricuspid insufficiency will appear.

Symptoms.—As long as the lesion is well compensated, these will be few. There may be some shortness of breath on exertion, but this is usually not marked. The same may be said of œdema and the symptoms due to venous engorgement. With loss of compensation, dyspnoea and cyanosis may both be marked, and œdema of the legs and the symptoms of passive congestion appear.

Physical Signs.—On *inspection*, the apex beat may be somewhat out to the left, and there may be quite marked heaving pulsation over the lower sternum and adjoining left costal margin, as well as in the epigastrium. If there is loss of compensation, the veins in the neck are full, and show pulsation, as described under tricuspid insufficiency. On *palpation*, a systolic thrill is usually felt at the base, sometimes over rather a wide area, or especially marked in the second left interspace. On *percussion*, the area of dulness is increased to the right. The most important signs are obtained on *auscultation*. A systolic murmur is heard, usually with its maximum in the second left interspace close to the sternum. It is sometimes propagated upward and to the left. The murmur is generally very harsh, often extends throughout systole, and seems more superficial and closer to the ear than that of aortic stenosis. It may be heard over a considerable part of the chest, but is not transmitted to the vessels in the neck. In some instances the murmur has been described as soft. The pulmonic second sound is usually absent or very faintly heard. A diastolic murmur is present if there be pulmonic insufficiency. The pulse does not necessarily show any change until loss of compensation occurs, when it is small, weak, and sometimes irregular. Clubbing of the fingers is sometimes present.

Diagnosis.—In this the great rarity of the lesion must be kept in mind, and it should always be the last to be considered; every other possibility should be gone over before this lesion is diagnosed, and even then it is safe still to have doubts. The murmur of aortic stenosis may cause error, but the fact of the murmur of that lesion being transmitted to

vessels of the neck is important. The pulmonary second sound is usually present in aortic stenosis and absent in pulmonary stenosis. The character of the pulse may help, that of aortic stenosis being suggestive. Certain congenital lesions may give difficulty, especially a patent ductus arteriosus, in which the murmur is often longer, and persists after the second sound.

Perhaps the most common error is to make the diagnosis on nothing but the presence of a systolic murmur in the pulmonic area. To keep in mind how frequently a systolic murmur is heard there without any valvular disease, is to lessen the chance of the error. Among these conditions of occurrence are (a) anemia, (b) peculiarities in the relation of the lung to the heart, (c) in many healthy young individuals, especially after exertion, in whom its occurrence may be difficult of explanation. In all of these the murmur is usually variable and altered, especially by change in position and respiration. The other signs of organic disease are wanting. Occasionally the murmur of mitral insufficiency is heard high up on the left side of the sternum, and may give difficulty. The other signs, and especially the accentuated second pulmonic sound, are of aid in recognizing this.

Prognosis.—This is grave, as a rule, although the rarity of the lesion does not allow of much deduction from experience. The condition of the right ventricle is most important. With any signs of its failing, the outlook is serious. One danger is the liability to pulmonary tuberculosis.

COMBINED VALVE LESIONS.

In nearly 50 per cent. of all cases the valve lesions are associated, either as a sequence, or two or more valves are affected at the same time. In the Edinburgh series of 1914 cases of valvular disease, there were 230 with a double aortic lesion, 231 with a double mitral lesion, and 362 with various combinations of aortic and mitral lesions.

The same cause may act on two valves; thus, in rheumatic fever in childhood the aortic and mitral segments may be attacked at the same time. Sclerosis may attack the aortic and mitral segments simultaneously. Occasionally an acute endocarditis involves the tricuspid as well as the aortic and mitral, and in a few instances all four valves are affected. A common association is insufficiency of the mitral valves as a sequence of lesion of the aortic segments. This relative insufficiency occurs so soon as the dilatation of the ventricle reaches a certain grade. In long-standing cases the tricuspid valves also become insufficient, and this is also a common sequence of stenosis and insufficiency of the mitral valves. Insufficiency of the pulmonary valves may also be combined with chronic lesions of the mitral. In consequence of the heightened pressure behind the chronic mitral lesion, sclerosis of the tricuspid segments may follow, with adhesion and gradual narrowing. The actual lesion of the valve is rarely pure stenosis or pure insufficiency. In the auriculo-ventricular orifices in particular, some degree of narrowing is usually present with the insufficiency. At the aortic orifices pure insufficiency of the arterio-sclerotic type is comparatively frequent.

In connection with combined lesions, one or two cardiac axioms are to be remembered. The rheumatic heart in children is very apt to have both valves on the left side involved. In adults, particularly in women, the lesion of the mitral is often single. In men aortic insufficiency may be the only lesion, to be followed as the heart enlarges by relative mitral insufficiency. Combined aortic stenosis and mitral insufficiency occur in a few cases of rheumatic endocarditis in young persons, and in later life is sometimes a consequence of chronic sclerotic changes.

As it is chiefly by the character of the murmurs that we estimate these combinations of valvular defect, it may be well here to speak of their indications. A diastolic murmur heard over the body of the heart with a direction of propagation down the sternum indicates insufficiency of the aortic segments. In a few rare instances insufficiency of the pulmonary valves is present. The murmurs produced during diastole at the auriculo-ventricular orifice have special characters and qualities. A pure systolic murmur heard anywhere over the body of the heart does not necessarily indicate a lesion of a valve. So numerous are the conditions under which it may occur that the single systolic bruit heard anywhere over the heart is of no moment as an indication of valve lesion. It must always be judged of in conjunction with other features. In any case the position of maximum intensity of the murmur, the direction of the transmission, the existence of hypertrophy of the heart, or of one special chamber, must be taken into consideration. Combined diastolic and systolic murmurs give a more definite indication of lesion of a valve. Heard at the base in an adult, we may be reasonably certain that the aortic segments are involved. Heard at the apex region, the indication of mitral valve lesion is not so definite. In a case of pure aortic insufficiency, the systolic murmur at the base may be caused by slight roughening of the segments or of the intima of the aorta, while at the dilated mitral orifice there may be a loud systolic and a rough rumbling presystolic (*E*nt murmur), and both associated with relative insufficiency. In such a case a single valve lesion is responsible for four heart murmurs. In general, it may be said that the diagnosis of combined valve lesions from murmurs alone is not very satisfactory. Much more important data are to be had from the study of the state of the individual chambers and the knowledge of the general cardiac pathology. In a child with an enlarged heart and a double murmur at apex and base, we are safe in diagnosing combined aortic and mitral valve lesion. In an adult man who has not had rheumatic fever, a similar combination may be produced by aortic insufficiency alone. Both in women and men mitral stenosis alone, or with insufficiency, may be the only lesion; but in cases of very long standing the valves on the right side of the heart are almost certain to be involved. As a rule, the physician is in a safer position if he limits his diagnostic ambition to two valves. Clinically, when lesions of three or four valves are determined with accuracy, mortifying postmortem disclosures are not unlikely to follow.

PROPHYLAXIS OF VALVE DISEASE.

That the profession as a whole scarcely appreciates the importance of preventive measures in disease of the heart is due in part to the fact

that full knowledge is not yet available, and in part to the difficulty in making efficient what we already have. There died of disease of the heart in England and Wales in the decade ending 1913 an average number of 1321.2 persons under the age of fifteen years and during the decade ending in 1923, 1040.7. As in many infections depending on faulty hygiene we see a clear diminution in the second period as compared with the first. If we exclude from this list the congenital cases, we may say that a large proportion of the remainder should come within the category of preventable disease. In four directions we may work toward the lessening of the incidence of heart disease: (1) In the all-important endocarditic group of the acute infections, rheumatic fever plays the important role, and we need a more careful investigation into the conditions under which this disease prevails. Two circumstances appear to favor it. The damp, unsanitary surroundings of the poor seem to be the factor in the chronic tonsillitis and pharyngitis to which so many children are subject. More and more the profession has come to the belief that the portal of entrance of the germs of rheumatic fever is the tonsils and adjacent pharyngeal tissues. Careful attention should be paid to the state of the nose and throat. A mouth-breathing child should be regarded as an unhealthy child, and enlarged tonsils and adenoids should be removed.¹ Damp houses should be regarded as unsanitary. There is no single problem of greater importance in preventive medicine than the reduction of the enormous waste of life in children in consequence of the rheumatic infection. (2) In a second group the cardiac breakdown follows overuse of the muscles. This is most often a myocardial affair, but in a considerable proportion of cases there is disease of the valve. In the large public schools, boys should be carefully examined before they are allowed to enter into athletic contests. In a growing heart, the developmental energies of which are taxed to the uttermost between the ages of fourteen and sixteen, it must be most hazardous to throw upon it the extra burden of providing a work hypertrophy. Both in schools and colleges much more stringent supervision should be exercised in the matter of athletics. In the occupations, heart disease has become less common. With the introduction of machinery the liability to strain of the heart has lessened. (3) Syphilis, as a cause of heart and arterial disease, plays a very important role, and the more efficient treatment now in general use should ensure a marked diminution of cardiac disease from this source. In the army and navy, more particularly, these preventive measures may be of service. Even in the community at large the proportion of individuals who have had syphilis is very large, and we all know the difficulty in ensuring proper treatment. (4) And lastly, all circumstances which lead to arteriosclerosis promote the sclerotic type of valve lesion. Hard work, alcohol, and overeating, particularly when combined with the high-pressure life, are very apt to lead to early degenerations.

Much may be done to promote the establishment of compensation and to postpone the final breakdown. In a rheumatic case with endocarditis it is to be remembered that it is not simply the vegetations,

¹ See Starling, *Guy's Hospital Reports*, London, 1923, p. 388; Hunt and Sinan, *Ibid.*, 1923, p. 383.

but the proliferative changes in the substance of the valve and the injury to the myocardium that have to be considered. The quiet life without strain and without special effort will enable a valve to heal with a minimum of damage. With the development of incompetency, it may take months before the heart adjust itself by hypertrophy to the new conditions. And the patient should be made clearly to understand the situation. It is always better to have a frank talk and explain the state of the "machine." Let it be expressed in mechanical terms, and make him understand that the difference between a healthy engine and his own is that in the former, for the ordinary purposes of life, only 25 per cent., say, of the horsepower is used, and there is a reserve of 75 per cent. to be called upon; whereas in his heart just the reverse conditions prevail, and while he may be perfectly comfortable using the 75 per cent. which he has to do for the ordinary duties of life, he has only a narrow margin of 25 per cent. for extra calls and emergencies. All circumstances that tend to depress vitality and to lower nutrition must be avoided, and he must be taught to adjust his life to his heart's capacity, or, in other words, to live within his cardiac income. For a young, energetic, muscular individual this is a hard lesson, and it becomes a serious problem how to adjust in proper measure exercise and diet, in the varied conditions in life.

TREATMENT OF CARDIAC INSUFFICIENCY.

During the establishment of compensation certain troublesome features are apt to arise which require treatment. It is not always easy to say just how far these depend upon the hypertrophy and dilatation themselves and how far upon associated neurotic states. Not infrequently we are consulted by young men or young women who complain of uneasy sensations about the heart with throbbing and palpitation, sighing respiration, and sometimes shortness of breath on exertion. On examination, signs of slight enlargement of the heart with overaction are present. This is really the well known irritable heart of the young, or some speak of it as developmental hypertrophy. Sometimes it would appear as if there was a disproportion between the growth of the heart and of the body. Overexertion, particularly in schoolboys and in young collegians, cigarette smoking, masturbation, and overuse of the bicycle are sometimes causes. A small number of these patients may be found to have signs of Graves' disease, apart from which the outlook is usually good. They should avoid overuse of the muscles and tobacco should be interdicted. They should be moderate in diet and the state of the heart should be carefully watched. It is not always well to make too much of the condition. Very often the unpleasant sensations of abnormal action are quickly relieved by lessening the diet, cutting off the more starchy articles of food and anything which causes flatulence. In other instances a few doses of spirit of camphor or aromatic spirit of ammonia may be needed, but, as a rule, all that is necessary is a careful regulation of the life.

Overcompensation is a condition not infrequently met with in the

early stages of valvular lesions before the heart has, so to speak, "found itself." Unpleasant throbbing, with irregular action, feelings of fulness in the head, inability to rest comfortably in the recumbent posture, are among the important symptoms, or the patient may have severe nocturnal attacks of palpitation. Very often this is not so much due to anything in the heart itself as the associated nervous state or anemia. Rest in bed for a week with careful regulation of the diet may be enough; if the heart's action is very violent, an ice-bag may be placed over the precordia for half an hour at a time. There are cases in which this unpleasant feature persists and is a source of more or less constant annoyance.

The actual valve lesion, of whatever nature, is very little under the control of treatment. Prolonged rest and potassium iodide influence the acute proliferative valvulitis, but we cannot replace scar tissue nor can we dissolve calcified atheromatous plaques. The whole treatment revolves about the *cardiac muscle*, the establishment and maintenance of compensation, the relief of the symptoms of insufficiency or decompensation, and the treatment of certain special symptoms.

1. **The Establishment and Maintenance of Compensation.**—Given a free coronary circulation, even with poor nutrition, the heart will gradually accommodate itself to the most severe valvular lesion. The hypertrophy and dilatation are not only salutary, but without them the circulation could not be maintained. As a rule, the call for additional strength comes slowly, and it is the old story of the woman who carried a calf in her arms every day, so that when it was an ox she still could carry it. So in the slow onward progress of a valvular lesion, month by month, year by year, the daily strength becomes equal to the daily needs. One point at the onset comes up in nearly every case: should the patient know of the existence of the disease? Most assuredly. It is impossible to carry out rational measures without his intelligent coöperation. The exceptions to this rule are very few. Occasionally a neurotic subject is upset and is frightened to perform the ordinary duties of life. Some individuals have a perfect obsession about the heart lesion, a sort of pantophobia which has made of them wretched valetudinarians. In many cardiac conditions, however, it is neither necessary nor advantageous to tell the patient of the state of his heart. In the hypertrophy of arteriosclerosis or of chronic Bright's disease, or of a chronic pulmonary affection, no special benefit is derived from laying stress on this feature of his case.

In the case of a young man, the first thing to be considered is his calling. Very often it has been at a special examination for some service that the valve lesion has been detected. Under these circumstances he is excluded from a certain number of occupations, and he should, if possible, choose one in which the demands upon the muscles are not great. In the working-class this is, of course, a great difficulty; but, if possible, trades and occupations requiring much exposure and hard work with the muscles should be avoided. In the higher classes, the professions with least strain, the clerical, the legal, and the occupations in which the work is sedentary, may be taken up. For persons with a

little capital, who have not themselves to do the heavy work, gardening and small farming are very suitable.

To maintain compensation the *diet* should be simple, avoiding, in particular excess of food. Often in the early stages the patients are anemic and feeble, so that they require an abundance of good food, with plenty of milk and eggs, meat, and fresh vegetables. If there is a tendency to put on fat, the diet should be restricted in carbohydrates and the patient should not be allowed to take too much food. Beer and spirits are quite unnecessary. In middle-aged men with aortic incompetency, if they have been accustomed to much spirits, a glass of whisky may be allowed at dinner. *Tobacco* may be used in moderation, but in young men it is best interdicted, so difficult is it to keep the use in moderation, and even two or three cigars or half a dozen cigarettes may cause irregularity. Tea and coffee may be taken in moderation, a single cup of coffee at breakfast and a cup of tea or coffee in the afternoon and another after dinner. No strict rule can be laid down about this, as even these small quantities may cause irregularity. The question of *exercise* is always the most important in connection with valvular disease, and it is not at all easy to reach a happy medium. In a great majority of well-compensated lesions, moderate exercise is of advantage. Regular systematic exercise, as in walking, easy cycling, horseback exercise, and golf, may be taken. For young men, the more violent sports and all competitive athletics should be interdicted. Golf is a particularly suitable game for men of all ages with well-compensated lesions. They should be warned not to overdo and not to play to the limit of tire, and the test of damage is the occurrence of dyspnoea or exhaustion. When outdoor exercise cannot be taken, systematic gymnastic movements may be employed. One is constantly asked, in the case of young girls, about *dancing*. With a simple mitral lesion perfectly well compensated and the apex beat not very far out, it may be allowed in moderation. Each case must be decided by itself. There are many instances in which it has not been at all hurtful. Hill-climbing and walking in the Alps may be very beneficial if not pushed to an extreme. After all, the test of any exercise is the result. If the patient is helped by it, if he is not made short of breath when at rest, or if it does not cause attacks of palpitation or nocturnal dyspnoea, it may be continued. As a rule, patients with valvular lesions should not go to very high altitudes. This is a good rule, to which, however, there are many exceptions. In a well-compensated mitral lesion there may be no difficulty. On the other hand, the patient may feel a good deal of distress at any altitude above 6000 feet.

Special care should be taken of the *bowels*, and if there is any tendency to corpulency an occasional saline purge may be used. The skin should be kept active by a daily bath. A cold tub in the morning may be taken if there is a good reaction afterward; if not, a lukewarm bath at night. Very hot baths should be avoided. Young people should be allowed plenty of sleep, and in the early stages of well-established compensation an hour's rest in the middle of the day is helpful. It is impossible to lay down hard-and-fast rules to meet every case, but the physician should try to reach the happy medium between overanxiety and unrec-

essary precaution, and allowing the patient a liberty which may lead to early decompensation. "Moderation in all things" should be the motto of the patient.

Two or three special points may be referred to. The question of *marriage* is always a distressing one, particularly if before the onset of the lesion the patient's affections have been engaged. Everything depends upon the lesion and the stability of the compensation. In young women with simple mitral incompetency there seems to be a minimum of risk. In many such cases they become the mothers of large families without the slightest damage to the heart lesion. It is to be remembered that often a lesion reaches a stationary point and the heart is really a first-class piece of mechanism, with only 50 per cent. less reserve than in a normal one. In one patient a mitral insufficiency followed rheumatic fever at sixteen. With a loud apical systolic murmur, and signs of moderate enlargement of the left ventricle, this woman had nine children and lived to be more than sixty years of age. The extreme mitral stenosis is not so favorable, and yet in many instances one sees repeated pregnancies safely carried through with quite advanced stenosis. Combined mitral and aortic disease, with great enlargement of the heart and tumultuous heaving of the chest wall and slight protrusion should interdict marriage. The middle-aged Lothario who is shocked to find (perhaps as the result of a life insurance examination) before the contemplated marriage that he has an aortic insufficiency, should be warned of the dangers. But these are cases in which, if the physician is wise, he will simply express an opinion on general grounds, as his specific advice is almost certain not to be taken.

In young persons special pains should be taken to prevent *intercurrent diseases*. In children the condition of the throat should be watched with the greatest care, and if there is the slightest enlargement of the tonsils it is better to have them thoroughly removed. The state of the mouth should be carefully watched, bad teeth removed, and a visit to the dentist should be paid once in three months. When possible, for a year or two after the establishment of compensation the patient should be carefully watched, and during the winter months a change of climate is most helpful—to Florida, Southern California, the South of France, Italy, Egypt, or Algiers.

2. Treatment of Loss of Cardiac Compensation.—At any stage in a valvular lesion, or in hypertrophy and dilatation of the heart from any cause, *acute cardiac insufficiency* may arise, associated with dyspnoea, more or less cyanosis, irregular action of the heart, gallop rhythm or embryocardia and a small, rapid pulse. In typical form this is seen in the cases of arteriosclerosis, in hypertrophy and dilatation from over-exertion, but it may occur in any form of valve lesion. It is the one condition in heart disease in which a venesection is advantageous. In many hands it is not satisfactory, because sufficient blood is not taken. Good results are rarely seen unless as much as twenty ounces is taken. To "breathe a vein" skilfully is now almost a lost art, and to get enough blood it is sometimes necessary to bleed from both arms. Hypodermics of ether in dram doses, strychnine hypodermically in $\frac{1}{30}$ or $\frac{1}{20}$ grain (0.002

to 0.003 gm.), or digitalin, $\frac{1}{20}$ to $\frac{1}{12}$ grain (0.003 to 0.005 gm.), may also be given, or strophanthin $\frac{1}{100}$ gr. intravenously. Camphor, either by the mouth (the tincture in dram doses) or hypodermically, in doses of 2 gr. (0.13 gm.) dissolved in olive oil, is useful. Local applications to the heart may be tried, a hot-water bag as hot as can be borne, or a mustard leaf. Probably the most certain way, however, is to inject a cubic centimeter of epinephrine (1 to 1000 solution) subcutaneously or directly into the heart.

In a majority of instances the failure in compensation is gradual, and it takes a week or two before the signs are well established. The first and all-essential requisite is *rest of the body* which may, indeed, be the only thing necessary. Time and again, to demonstrate its importance to students, the senior author treated patients with this measure alone, combined, perhaps, with a brisk saline purge, and within a few days the œdema of the feet disappears, the bases of the lungs become clear, and the heart's action quiet and strengthened. In many instances the chief value of a consultation has been in the insisting upon absolute rest. It is not always possible to induce a patient to go to bed, nor is it always possible for him to remain in bed. In the milder grades of cardiac breakdown the semi-recumbent posture may be maintained, but it too often happens that the condition is one of orthopnœa, and there is no possible position of comfort in bed. The patient then has usually to sit up out of bed, and he is fortunate if there is available an old-fashioned "grandfather's chair" with the comfortable side pieces for the head. One of the greatest difficulties in the nursing of these cases is to get a position in which the patient may sleep comfortably. Too often just as he drops off, the head falls and he awakens with a start. An ingenious nurse may sometimes be able to devise methods for the support of the head, but it is by no means easy. Sometimes these patients get into all sorts of remarkable attitudes. One poor fellow with a cardiac breakdown following emphysema had comfort only in the knee-elbow position. Patients may be able to sleep kneeling at the side of the bed. One man for weeks could get relief only by leaning forward on to the back of a chair against which he rested his forehead, on which, in spite of every precaution, he had a bedsore. The greatest care should be taken of the back to prevent bedsores. Sooner or later, there comes a stage when there is more or less permanent cardiac insufficiency which neither rest nor medicinal measure is able to overcome. The patient is tired of bed, and under these circumstances it is often beneficial to let him be up and about for part of the day, even if the exercise does increase the dyspnoea. In these chronic cases, when possible, the bed should be wheeled out-of-doors, or they may sit up on a couch on the veranda for part of each day, or be taken out in a wheeled chair. The question of systematic exercise will be considered in connection with the special methods of treatment.

Diet is one of the most important and at the same time difficult elements in the treatment. We have all been notorious sinners in over-feeding our heart patients, particularly in the stage of broken compensation. The stomach is not only a near but a bad neighbor to the heart. With venous stasis of the gastric mucosa it is impossible to have a good

gastric juice, and it is a good rule for the first few days, when the patient comes under treatment, to give a minimum quantity of food until with saline purges, the overloaded viscera are relieved. A patient will get along perfectly well with the whites of six to ten eggs, flavored with lemon; this is very palatable, and in three or four of the feedings a little whisky or brandy may be given. Freshly prepared beef juice, milk diluted with lime-water or soda-water, and whey are also suitable. Not too much should be given, and when there is nausea or vomiting it will do no harm to let the patient go for twelve hours without any food in the stomach, and at intervals very hot water may be given, and if it be thought necessary, rectal enemas may be used. All prepared starchy foods are, as a rule, contraindicated. Patients differ very much in their tastes and gastric capacities, and to a certain extent these may be humored. As soon as possible the patient should be taken off the "slops" and given solid food in small amounts; care should always be taken not to fill the stomach too much with liquids and solids at the same time. The sensible doctor will not forget that even a perfectly healthy stomach could not stand the heroic medication which we sometimes encounter, three mixtures—necessitating a dose at least every two hours, often a nocturnal pill, the nocturnal purge, the morning saline and sleeping draught at night. Too often this Arabian polypharmacy defeats the very object we have in view.

Reduction of Intake of Liquids.—It is by no means easy to decide just in what class of cases liquids should be restricted. Theoretically, the ingestion of large quantities of fluid increases greatly the work of the heart, but there are many conditions in which it seems necessary in order to promote diuresis and sweating to give large quantities of fluids. The following may be taken as indications, but they must be modified to suit the conditions. When compensation is good the patient should be careful not to take too much liquid, but the quantity of urine should not be allowed to fall below a normal limit. Such patients should not be allowed to take "cures" indiscriminately, as the drinking of very large amounts of liquid may lead to pronounced embarrassment of the heart. In very stout patients with valvular or myocardial lesions, the meals should be taken as dry as possible, and fixed quantities of liquid given during the day, enough to keep up the output of urine. The cases which demand reduction of the liquids are those with cardiac dilatation and venous stasis and oedema. Combined with purgatives, the reduction in the total of the liquids to $1\frac{1}{2}$ pints given at stated intervals, either milk and soda water or milk and barley water or albumin water, may have a very beneficial effect on the dropsy and promote the flow of urine.

Special Methods.—Certain plans of treatment have been introduced—combinations of diet, exercises, and baths.

Oertel's Method.—He sought to reduce the quantity of blood and to diminish the amount of fat. The treatment consists in, first, the reduction in the amount of liquid to about 36 ounces in the twenty-four hours, which includes the amount taken with the solid food. Baths and sweating help still further to reduce the quantity of water in the body. Secondly, the diet, which is chiefly protein:

Morning.—Cup of coffee or tea, with a little milk, about 6 ounces altogether. Bread, 3 ounces.

Noon.—Three to 4 ounces of soup; 7 to 8 ounces of roast beef, veal, game, or poultry; salad or a light vegetable; a little fish; 1 ounce of bread or farinaceous pudding; 3 to 6 ounces of fruit for dessert. No liquids at this meal, as a rule, but in hot weather 6 ounces may be taken.

Afternoon.—Six ounces of coffee or tea, with as much water. As an indulgence an ounce of bread.

Evening.—One or 2 soft-boiled eggs; 1 ounce of bread; perhaps a small slice of cheese, salad, and fruit; 6 to 8 ounces of wine with 4 or 5 ounces of water. The third and most important are exercises, the so-called "*Terraincur*." Graduated walking exercises are taken, not on the level, but uphill at various grades. A definite amount is done each day and the distance is gradually increased. Undoubtedly, at proper resorts suitable cases are greatly benefited by this plan of treatment, but it is to be borne in mind that Oertel recommended it particularly for stout individuals with weakened heart action.

Nauheim Method.—Here the great influence is believed to be effected through the stimulating influence upon the heart of hot CO₂ saline baths combined with special muscular exercises. The heart is stimulated to more vigorous contraction and the area of heart dulness is diminished. By reducing the temperature of the bath and increasing the concentration of the salts, the heart's action is still further stimulated, and it becomes progressively strengthened. Resistance exercises are given by a trained attendant, and definite groups of muscles are systematically brought into action.

The senior author watched carefully the results in many patients who were under treatment at Nauheim. They may be divided into three groups: Scores of persons who have nothing whatever the matter with their hearts are greatly benefited by the change and the holiday. In a second large group much damage is done. For years the senior author was in the habit of seeing victims of the Nauheim cure, many of them physicians, who had come for advice regarding the long train of troublesome symptoms of the neurotic heart. Frightened by a little irregularity, they submitted themselves to a Nauheim "cure," and were greatly alarmed to find that instead of improvement, they had grown worse. In many neurotic women the last state was much worse than the first. As a rule, these patients are little if at all benefited. Cases of aneurism, valvular disease in the late stages of broken compensation and arteriosclerosis with high pressure do not seem to do well under this method.

A third group, in which good results are seen, comprises the chronic myocardial cases, the fat patients with weak hearts, and the cases of valvular disease with slight disturbances of compensation, but not with dropsy. The baths may be carried out at home, but the same beneficial results are rarely obtained, even in suitable cases. As so often happens in these special forms of treatment, an opportunity is given for unscrupulous practitioners to impose upon patients, and the Nauheim method has not always been carried out with common-sense. A pitiful lack of judgment has characterized the treatment of many cases. One thing

should be demanded of those who carry out the treatment at Nauheim or elsewhere: they should stop alarming people who have little or nothing the matter with their hearts.

Drugs Which Help to Restore Compensation.—Among these *digitalis* not only takes the first rank, but is in a class apart. Evidence has been accumulating to show with much greater accuracy the effect of digitalis on the various functions of the heart. *Excitability* is not a function which is affected to the same degree as the others, yet the frequent presence of *pulsus bigeminus* is evidence of a hyperexcitability of the ventricle and the production of an extrasystole in the more rhythmic parts of the ventricle. The second beat in *pulsus bigeminus* is never preceded by an auricular beat. Digitalis occasionally causes extrasystoles to disappear. When the drug causes their appearance, either irregularly or in the form of a coupled rhythm of the pulse, it is evidence according to Norris, of calling upon the cardiac reserves, and though improvement may be manifest the drug should be stopped.

The effect of digitalis on *contractility* is one of the greatest dangers of its action. This may give rise during the earlier stages to the condition known as *pulsus alternans*. If its action is allowed to continue, it produces half the rate of beat in the arteries, the second beat being unable from its feebleness to produce a wave in the arteries. Later the second beat may be entirely suppressed even at the heart. Wenckebach's explanation is that the normal depression of contractility which follows each beat is much greater under the action of digitalis, and that when the second stimulus from the auricle reaches the ventricle the latter is only able to respond in a feeble manner. In certain cases digitalis has caused *pulsus alternans* to disappear.

Conductivity is markedly depressed by digitalis. When such an effect is present, it takes the form of lengthening the interval, normally about one-fifth of a second, between the beginnings of the auricular and ventricular impulses. This may go on to heart-block. But in some cases digitalis does not produce an effect on conductivity, unless given in enormous doses, which points to involvement of other factors. Of the effect on *tonicity*, there is the invariable clinical observation that it is of the greatest use when dilatation is present, and the benefit which comes from it is due to a stimulation of this special function of the heart muscle.

Digitalis is indicated in all conditions in which the muscle of the right side of the heart is at fault; in dilatation of its chambers; but preëminently when there is auricular fibrillation or if there be shortness of breath, cyanosis or œdema. The type of valvular lesion makes no difference whatever, as the cardiac insufficiency, for which the digitalis is almost a specific, is an affair of the muscle, not of the valves. In the common, triple combination characteristic of insufficiency—*dyspnœa*, venous stasis and dropsy—experience has fully borne out the ninth inference of Withering, "that digitalis has a power over the motion of the heart to a degree yet unobserved in any other medicine." In the arteriosclerotic form of auricular fibrillation its action is uncertain.

In cases of acute cardiac insufficiency the good effects are not so striking, the patients admitted in a state of cyanosis and *orthopnœa* and

embryocardia are much more promptly relieved by copious venesection. The results of the administration of the drug are often phenomenal. The patient, who has been in a desperate state, may within a few days be rendered comfortable.¹ Relief of the thoracic oppression and of the dyspnœa, lessening of the cyanosis, and increase in the flow of urine are the indications of beneficial action. It may also be used and with benefit in paroxysmal auricular fibrillation, some cases of paroxysmal tachycardia and cases of *pulsus alternans*.

The *contraindications* for the use of digitalis are much more numerous than the indications. Few valuable drugs are so much wasted. Neither rapidity of action nor arrhythmia are in themselves indications, unless accompanied by signs of weakness of the muscles. There are many cardiac irregularities over which digitalis has no control, and persistency of irregularity is neither a contraindication nor an indication for its use. In many cases the signs of heart failure in mitral disease disappear under its use, while the irregularity persists. It may be said broadly to be contraindicated in all forms of heart disease without symptoms of muscle weakness; it is contraindicated, too, in the great majority of cases in which the patients come complaining of irregular and violent action of their heart. Such cases are much more satisfactorily treated by attention to their digestion and the nervous conditions. In states of high arterial tension, one is sometimes in a quandary, as the paradoxical features may be presented of a dilated heart with gallop rhythm and blood-pressure considerably above the normal. Under these circumstances the latter may be discounted. But in middle-aged men with permanent high tension, sclerotic vessels, and a hypertrophied left ventricle, digitalis may be directly hurtful. In angina pectoris, as a rule, the underlying conditions are not those which are modified by digitalis. In a few cases in which the heart's action is feeble, gallop rhythm is present, and particularly when the angina is directly associated with a very old valve lesion, more particularly in mitral cases, digitalis may be used without risk. In aneurism the drug is not of any service, except in rare cases when the dyspnœa and œdema are directly due to heart weakness. There is widespread belief in the profession that digitalis is contraindicated in insufficiency of the aortic valves. In the periods of decompensation the drug more frequently fails than in corresponding mitral cases, and we more frequently see death in heart cases in aortic insufficiency during the administration of digitalis; but this is particularly in the arteriosclerotic group when the nutrition of the heart muscle is failing, and when the coronary arteries are seriously involved. In a majority of instances just as good results are seen in this lesion as in mitral cases, but a little more care has to be exercised in its use.

With the common gastric disturbances of broken compensation, digitalis, as a rule, is not well borne, as it often aggravates nausea and vomiting. Under these circumstances it is much better given hypo-

¹ For the young physician there is no other reputation-producing medicine of the same rank with digitalis, and it is one of the dozen drugs the uses of which repay a lifelong study. How he uses it may be taken as a sort of indication of the therapeutic intelligence of the practitioner.

dermically. Toxic symptoms, which are not very often met with, follow the employment of very large doses or, occasionally, the prolonged use. Nausea, vomiting, sometimes diarrhœa, with pallor of the face, feeble, rapid pulse, and diminution of the amount of urine are the special features. There are three useful indications when the patient has had enough digitalis. The pulse becomes slow, but it must be remembered that one of the characteristic actions of the drug is the production of the bigeminal pulse. The second beat may become feebler, and finally is not perceptible to the finger. It may at the same time be evident as a small beat in the tracing, and the corresponding sound may be heard at the apex. The pulse may be counted at 40 when the heart beats are 80, or at 60 when they are 120. Mackenzie, Hewlett, and others have studied this peculiar action of digitalis, which may produce a definite type of heart-block. Hewlett reported cases which seem to show that the combination with atropine prevents this effect. The condition is common in mitral cases, and may keep up for weeks without any special risk, but it may be followed by a rapid feeble action of the heart. The second important indication is a lessening of the flow of urine. Directions should always be given to measure and record the daily quantity, as a reduction gives one of the earliest indications when the useful action of the drug has ceased; and thirdly, a progressive lowering of the blood-pressure is, as a rule, an indication to stop the drug.

Mode of Administration.—The judicious practitioner will use three or four preparations which have stood the test of many years and look askance at many of the new-fangled preparations of the drug.

The Tincture.—In a patient with mitral or aortic lesion, who has just begun to have shortness of breath with swelling of the feet and diminution of the amount of urine, a good plan is to give the tincture in 15 minim doses every four hours for two days. Then it may be stopped for twenty-four hours and resumed for another two or three days, and so continued at intervals. Usually within ten days or two weeks the serious symptoms have disappeared and the drug may be stopped, or continued in 5 minim doses three times a day. As a rule, the tincture answers admirably, unless the stomach is very irritable. In cases when it is desirable to get the maximum action in the shortest time Pardee¹ has shown that the tincture may be given in relatively enormous doses. In doses of 4 or 5 drams, its full action may be obtained in five or six hours and the effect will last ten days. The maximum dose is calculated by assuming 2 minims for each pound of body weight. In order to avoid dangers due to idiosyncrasy it is safer to give 1-drain doses for 4 or 5 doses at intervals of four hours. The signs indicating that a full amount has been given are a slow pulse or vomiting.

The *infusion* in $\frac{1}{2}$ ounce doses, four to six times a day, is equally efficacious, and is believed by some to be more diuretic in its action. When the stomach is irritable it is not so well borne.

Powdered digitalis is of great service either alone or in combination with squill and mercury, 1 grain of each in the form of the Addison or Guy's pill.

¹ *New York Med. Jour.*, 1919, 2, 1064.

The latter is particularly indicated in the cardiac failure of old arterio-sclerotic patients, those with chronic nephritis, and more particularly when there is swelling of the liver, ascites, and jaundice.

The so-called active principles of digitalis have been much used but are rarely of particular value.

For how long may digitalis be used without danger? There is not much risk of cumulative action with sudden untoward manifestations. As a rule, the symptoms above referred to suggest at once that the patient has had enough. Twice the senior author knew the digitalis habit to be contracted, in which over a long period of years patients took the tincture, in one case of 5 and in the other 10 minims two and even three times a day. One was a physician with aortic insufficiency, who had taken digitalis daily for more than twenty years as he had a fixed idea that without it his heart became feeble.

Quinidine sulphate, if digitalis has failed to restore the cardiac rhythm, should be tried in doses of 3 to 5 gr. twice or thrice daily. It is specially valuable in those cases in which after œdema and cyanosis have disappeared the rhythm is still irregular. In a senile irregular heart with disordered rhythm it is not so useful.

Epinephrine though a most valuable drug has the disadvantage that it must be injected subcutaneously to be effective. This is no bar in hospital cases and in those in which digitalis is unsuitable or has failed, the solution of 1 to 1000 may be used twice daily. It is well to proceed very slowly because clots in the auricular appendix are apt to be dislodged and produce embolism.

Substitutes for Digitalis.—*Strophanthus* may be used in the form of the tincture, of which 10 minims (0.6 cc.) may be given every three or four hours. Its constricting effect upon the smaller arteries is said to be less than digitalis. It is very often useful to keep up the action of the heart after a course of digitalis, and in children with old mitral lesions it is sometimes better borne. As a rule, it is rarely efficacious when digitalis fails. *Strophanthin* has been used for obtaining the same end as digitalis, either preliminary to a course of this drug or in case the reaction of the heart to it has failed. It is injected intravenously in doses of from 0.1 to 0.5 milligram and may be given intramuscularly in the same doses. The cases should be carefully chosen and it should not be given in chronic nephritis. Twenty drops of the tincture has been taken daily for two years without harmful effect. *Sparteine sulphate*, in 1 gr. doses, *adonis vernalis*, and *convallaria* may be sometimes useful. Camphor has a reputation in some quarters; caffeine and theobromine are recommended, but in failure of the heart muscle they are not of much value in comparison with digitalis. Strychnine by mouth or hypodermically in acute conditions may be of service. Depending on the condition, it may be given in doses of $\frac{1}{60}$ to $\frac{1}{20}$ gr. (0.001 to 0.003 gm.). *Alcohol* appears to have no stimulant action on the heart; but by its action as a vasodilator it may be of great value in failure with high tension.

The Use of Morphia.—In the late stages of cardiac failure when the symptoms are wearing out the courage and power of the patient and giving the doctor a sense of utter helplessness morphia by giving tempor-

ary rest produces effects that give a new resistance and hope to the patient. While it is contraindicated with a low output of urine and the presence of a great deal of bronchial catarrh, it is perhaps next to digitalis the most favorable drug in the treatment of the heart itself. In the cardiac failure of arteriosclerosis, with the terrible nights of orthopnoea, "cardiac asthma" and restlessness, hypodermics of morphia give the greatest relief. It is of great value in progressive failure of the left ventricle with unrelieved respiratory distress and in acute pulmonary œdema. We are, altogether too cautious in the use of this drug, which is of incalculable service in the severer manifestations of the disease. Given in small doses of $\frac{1}{8}$ gr. (0.008 gm.) hypodermically it may be repeated in a few hours if rest is not obtained. In children paregoric is very helpful, and it may also be used in the attacks of nocturnal palpitation in the irritable heart.

3. Treatment of Special Symptoms.—Cardiac *dropsy* is usually relieved by digitalis. When resistant, it is most difficult to overcome. The use of the saline laxatives, particularly the salts given in concentrated form early in the morning, the compound jalap powder, or calomel purges, are very helpful. To promote sweating, hot baths, either the very hot tub, the steam bath, or the hot-air bath, may be tried cautiously. On the whole, it may be said that this is not so satisfactory in cardiac as in renal dropsy, and it is sometimes very difficult to get a profuse action of the skin. The hydrothorax and ascites may require tapping. If the anasarca of the legs becomes very great, the skin may be punctured with small needles, or small incisions made in several places. Dressed with gauze and thick layers of sterilized cotton, an enormous amount of fluid may be drained away. It is, as a rule, perfectly safe when the usual precautions to avoid infection are taken. In milder grades of the anasarca it is very helpful to bandage the legs firmly.

The use of theocin (gr. v, 0.3 gm.) is worth a trial. Novasurol has been used extensively of late but its use is not without danger if there is renal disease.

Sleeplessness and Restlessness.—With failure of compensation the patient has almost always bad nights, and the question of the use of hypnotics comes up at an early date. It is well at first to try the milder forms. Paraldehyde is often very satisfactory, given in dram doses; the patients become accustomed to the unpleasant odor. Veronal, trional or pheno-barbital alone or combined with potassium bromide may be tried. Chloral hydrate is often useful. When the milder hypnotics fail, as they often do, opium should be used. Cases of cardiac asthma may be benefited by bleedings and a vegetarian diet.

Anemia.—This should always be kept in mind, and if present, iron and arsenic should be given as soon as the acute cardiac features are over. Some patients are greatly helped by occasional courses of these drugs.

Cyanosis.—Cyanosis with great respiratory distress, especially when due to bronchitis, often receives immediate relief from a prompt venesection of half a pint to a pint.

CHAPTER XX

FUNCTIONAL DISEASE OF THE HEART

By CHARLES F. HOOVER, M.D.

FUNCTIONAL disease of the heart may be defined as cardiac symptoms that originate wholly from psychic disturbances or a more comprehensive view may include symptoms that are traceable to disturbances of the heart's innervation through abnormal stimuli that have their origin in causes which lie quite outside the field of consciousness, but are nevertheless produced through disordered function of the same nerve supply. Introspection, bulbar disease, mediastinal disease, disease of the cervical cord, digestive disturbances in the upper alimentary tract, and pelvic diseases may all produce cardiac symptoms that are very similar.

In former years the relation between disturbed endocrine function and the heart was not comprehended as now and no doubt we formerly believed many cases to be hysterical, psychasthenic or nervous that we now classify as Graves' disease or myxœdema. Many such cases have been rescued from the stigma of functional neurosis by the modern advancement of knowledge of metabolism. Although many cases formerly classified as functional heart disease are now believed to be organic or due to causes that lie quite outside the field of consciousness, we are still in a quandary to account for cardiac incompetence and heart death by what is found in most careful autopsy studies.

The most refined histological methods that have been devised for the study of nerve paths often fail to throw light on grave functional disturbances which we believe to have their origin in disease of the heart's nerve supply. Since the cardiac ganglia and the manner of wave transmission within the heart have been studied by the electrocardiograph many cases of arrhythmia have been taken out of the realm of functional disorders and given a pathological physiology formerly quite beyond our clinical ability. However, it is doubtful if we are justified in denying a purely psychic source to some disturbances of rhythm merely because we can locate an anatomical structure whose functional misbehavior causes the symptom. The exact pathological physiology that invokes the misbehavior may rest on a psychic basis quite as securely as formerly when the auriculo-ventricular mechanism was less understood.

A good example of this is a patient I have observed at frequent intervals for twenty-seven years. The patient is now sixty years old and in excellent health, but for many years she had attacks of paroxysmal tachycardia in which the rate would go suddenly from 80 to 220 per minute and continue there for an hour or more, and then just as suddenly revert to the normal rate after eructation of gas from the stomach. On one occasion, in 1898, the heart-rate fell suddenly to 15 per minute and

was arrhythmic while the bulbus venosus revealed very rapid pulsations. The attack lasted as long as the previous attacks of tachycardia and terminated in the same manner after the eructation of gas. There was persistent fear of fatal organic heart disease until 1905, when it was found that the tachycardia could be stopped when the patient was inverted while she took a deep breath and made a prolonged expiratory effort with the glottis closed. This experience convinced the patient that she did not have organic disease and there has been no return of the auriculo-ventricular tachycardia or the auricular tachycardia with ventricular heart-block which the electrocardiograph would certainly have shown. The long period during which these attacks occurred and the sudden cure that attended suppression of fear is quite convincing that the attacks were genuinely functional, without an organic lesion and that they were due to disturbed mental and emotional causes.

In another patient observed for fifteen years there have been several attacks of auricular fibrillation with demonstrable enlargement of the right auricle during the attacks. The duration of the fibrillation has been from half a day to three days. The patient is a very nervous, sensitive and introspective man in whom the attacks can always be traced to business worries and anxiety. Between the attacks there is absolutely no evidence of cardiac disease. These two cases suffice to prove that without organic disease of the heart or cardiac nerves there may occur exactly the same kind of disturbance in the auriculo-ventricular mechanism that in recent years we have learned to picture in our minds as a bit of pathological physiology based on anatomical disease of the heart.

To predicate organic disease of the heart on a functional basis is, however, a very doubtful procedure, for since the modern development of our conception of endocrine function it is probable that many cases we formerly believed to reveal cardiac dilatation and incompetence as a direct result of disturbed cardiac innervation, we now commonly diagnose as Graves' disease and occasionally as myxœdema. As I review in my mind some of the patients who in former years were believed to have cardiac dilatation and hypertrophy as a result of psychic and emotional disturbances and sexual disorders, it seems probable that if they were now to pass under review we would recognize them to be either Graves' disease or due to syphilis.

We dare not accept emotional or psychic causes for disordered heart function that is attended with cardiac dilatation, compensatory dilatation or hypertrophy. With such evidence we can now find a better explanation than functional disease, although there may be a purely functional origin for disturbances in rate and rhythm of the auriculo-ventricular mechanism. If, however, there is disturbance only in rhythm and no change in the size of the heart's chambers and no demonstrable impairment in the blood flow we are not justified in assuming that there is no organic disease of the heart, for at autopsy we see very marked anatomical disease of the heart that does not modify the size of either ventricle or auricle.

Abnormal Precordial Signs Not Due to Disease.—Of all the abnormal signs detected over the precordial area a murmur is the most common. A murmur is due to eddies in the blood current that produce sufficient

vibration to become audible. An eddy is due to the arrival of a vein of air or fluid of a high velocity into a field of a lower velocity. The difference between the velocities of the two currents must attain a certain magnitude before the eddies produce an audible sound. The simplest illustration is to partly compress a femoral artery and auscult the murmur of stenosis that is audible distal to the compressing finger. If the blood flow is adequate with sufficient pulse-pressure so that the vein of fluid passes the stenosis with sufficient velocity into the field of low pressure distal to the stenosis there will be an audible murmur, but if the pulse-pressure is small and the blood flow sufficiently reduced no murmur can be heard.

A man, aged sixty years, with cardiovascular sclerosis, developed asystole. The heart-rate was 160 and the arterial pressure 150/120. When the femoral artery was partly compressed by the examiner's finger no murmur could be heard beyond the stenosis simply because the small volume flow and the high diastolic pressure distal to the compressing finger lowered the difference in velocity between that at the stenosis and in the field beyond it, that consequently the eddies were insufficient to produce an audible sound. Not only must there be a suitable conformation of the channel but also an adequate difference in velocity between the two veins of fluid to produce the murmur.

The mechanism of the murmur of stenosis and that of insufficiency is the same. The murmur of dilatation in a vessel is very similar but not identical with it. When a murmur of dilatation occurs in aneurism there must be a sudden transition from a smaller to a larger lumen to procure eddies of sufficient vigor to become audible. If the transition from the normal lumen to the widest part of the aneurism is gradual, as in the fusiform variety of the descending aorta, there will be no murmur although the aneurism may be of sufficient size to erode several ribs and project as a pulsating tumor in the left interscapular region. There are always two factors necessary for the production of an audible murmur, viz., suitable conformation of the channel and adequate velocity of the current.

The wonder is not that murmurs occur in the heart, but that under the usual normal conditions they are absent. At autopsy we often find no anatomical evidence on which to base the origin of a murmur that we located at one of the auriculo-ventricular or arterial orifices, yet during life there must be either a change of the conformation in the channel or an acceleration of the current's velocity to produce eddies sufficiently strong to become audible. It is conceivable that in the passage of blood from the right conus arteriosus to the pulmonary artery there may be a sufficient difference in velocity between the central and peripheral part of the current so that the mingling of the two will produce audible eddies. This location is cited because it is very common to hear there an endocardial murmur when we examine patients who have diseases in which there is an acceleration of the blood current through the heart, *e. g.*, primary anemia and Graves' disease. There is, however, another way in which precordial murmurs can be produced that are not endocardial. These *cardio-pulmonary* murmurs were first clearly expounded by Potain nearly forty years ago, but their frequency and deceptive significance have received little attention in medical literature. They are very com-

monly heard in children and during adolescence. They may be systolic or presystolic in time and occur most frequently over the right conus arteriosus where the forward systolic projection of the cardiac area is strongest. A cardio-pulmonary murmur may be so loud as to be plainly audible 6 inches from the chest wall. In one instance the nurse observed it without applying the ear to the chest. She asked "What is the funny noise in the heart?" The patient had bilateral thoracic empyema because of which a part of the lung was crowded over the precordial area. There was a loud rasping systolic murmur heard over the entire precordial region which was very tympanitic to percussion. The autopsy revealed a tongue of lung in front of the heart and a perfectly normal pericardium and normal heart.

The conditions for the production of a cardio-pulmonary murmur require that the precordial lung should be sufficiently compressed during the forward excursion of the heart so that the displaced air passes from the air cells into the bronchi with sufficient velocity to produce audible eddies. At first view this manner of producing an intrapulmonic murmur may seem to be at variance with the source of the respiratory murmur heard normally over the surface of the lungs. There is ample proof that the normal lung murmur is merely the transmitted vibration produced by the passage of air through the glottis. Beyond the glottis there are only two locations in the air path that have a conformation suitable for the production of a murmur, and these are in the small bronchiole as it opens into the antrum of a lobule of the lung and the small bronchiole as it branches off the larger bronchus. The former of the two is where affluent air and the latter where effluent air can produce murmurs. The conformation is suitable but under normal respiratory conditions the velocity of both affluent and effluent air in these parts is insufficient to produce audible eddies in the air current. The following consideration will show why this is true. If in the same time 1 litre of inspired air passes the glottis, 1000 cc. pass the collective terminal bronchioles, the velocity in the bronchioles will be inversely proportional to that at the glottis as the collective area of all the lumina of the bronchioles exceeds the area of the glottis. It would be a conservative estimate to say this proportion is 1 to 100. Consequently in normal respiration the velocity of the air current is insufficient to produce an "alveolar murmur" although the conformation is suitable for it. However, when a tongue of lung is compressed by the forward thrust of the heart, the displacement of air may be rapid enough to afford a velocity that is sufficient to produce a murmur. The cardio-pulmonary may sometimes be easily differentiated from an endocardial murmur, but at other times this may be uncertain. The cardio-pulmonary murmur "dies on the spot." It is not transmitted along the chest wall nor along the vessels leading off from the heart. The murmur may often be recognized as having a superficial origin and its quality may be rasping so that it occasionally resembles a pericardial friction sound, and a crepitation may be palpable over the site of the murmur. The murmur is synchronous with the forward thrust of the heart and is not bound to the time of closure of the atrio-ventricular or opening of the semilunar valves. The murmur, therefore is heard in the

middle of the short pause. It may begin after the systolic and cease before the diastolic sound is heard. It may also be heard during the pre-systolic excursion of the heart.

The cardio-pulmonary murmur often disappears when the patient changes from the upright to the lying or from the lying to the upright position. The cardio-pulmonary murmur may be made to disappear during a forced expiratory effort, or during a maximum expiration the murmur may take on a superficial rasping character that clearly betrays its origin. Or the murmur may be silenced with an inspiratory filling of the lungs. In fact any procedure that will reveal the dependence of the murmur on a suitable thickness of lung between the chest wall and the heart assists greatly in the differentiation.

When all these precautions are observed there still may be doubt as to the extra- or endocardial origin of the murmur. If one's diagnostic resources are limited to the audible phenomena he will often commit the error of diagnosing heart disease in the presence of a normal heart. A medical consultant often has such cases referred to him for an opinion when life insurance is in question, and on several occasions the writer has seen healthy children put to bed on account of a cardio-pulmonary murmur. These murmurs are most often located at the left border of the sternum in the second and third interspaces directly over the right conus arteriosus; next in frequency are those heard over the apex of the heart.

Volume Flow, Blood Volume and Blood-pressure.—Thus far there have been no satisfactory methods devised for estimating either the volume flow of blood through the heart or the amount of endovascular blood. Yandel Henderson's ethyl-iodide method is the most recent and probably comes nearer to providing a dependable method for estimating the volume flow than any so far that have been tried. Thus far there has not been sufficient trial of the Henderson method to prove its clinical value. Should a device for this purpose prove successful it will add more to the exactness of clinical studies of the circulation than all other precise methods have contributed to the subject.

Of the two problems, volume flow and endovascular blood volume, the former is more tangible and is attended with fewer difficulties than the latter. To estimate cardiac outputs we have a tangible cardio-respiratory function in the blood ventilation in the lung which provides a source for attacking the problem of blood flow through the pulmonary circulation. Should this be quantitatively estimated we would have a precise method for learning the cardiac output per minute and for each systole. The difficulties in the way of making this estimation have not yet been surmounted, but the prospect is hopeful because it is only problems of technique that have to be overcome, whereas in the problem of blood volume we have anatomical and physiological variables to deal with that complicate the simple device of estimating the dilution of pigments injected into the blood stream. The endovascular volume is subject to rapid and many variations and large amounts of blood may be temporarily stored in the spleen, alimentary tract and liver and emerge from its shunted location into the actively circulating blood in a short space of time, consequently we are not safe in making the inference that a few

cubic centimeters of pigment injected into a vein become uniformly diffused through the whole blood volume. In this problem we meet other difficulties than those of technique in the variable vascular volume and blood distribution which are the very things we wish to evaluate.

With our present knowledge we are left to arrive inferentially at a mental estimate of cardiac output and blood volume from a study of blood distribution, diastolic-systolic excursion of the heart, the size of the heart's chambers and maximum and minimum arterial pressure. If these observations are critically done we can gain a clear idea about the blood hydraulics and inferentially form an idea as to whether the heart's output is increased or greatly diminished.

In the past thirty years arterial pulse-pressures have been measured routinely and this has furnished a large amount of information and enabled us to record quantitatively what we formerly observed qualitatively. The clinical inferences drawn from the measurement of blood-pressure are often too far reaching and too hastily drawn. A rise in blood-pressure is often translated as meaning arteriosclerosis when there may be only a transient arterial hypertonus and sometimes the hypertonus may be only in the arms when the pressure is measured and a high end-aortic pressure is wrongly inferred. Before the reading of the brachial blood-pressure is accepted as a measurement of aortic pressure we should always estimate the pressure in the femoral artery by manual palpation. This artery varies little in size with changing vasomotor arterial tone; it lies on a firm bony background and is covered with a thin layer of subcutaneous fat. The end-pressure in the femoral artery is the lateral pressure in the abdominal aorta. Therefore the conditions are very favorable for palpation of bursting tension which in the femoral artery varies directly with the pressure. If this method is routinely followed for critical control the sphygmomanometer will often be found incorrect.

A striking example was in a woman, aged fifty years, who had suffered from severe attacks of angina pectoris for fifteen years. The brachial pressure had been frequently measured and always found to be between 200 and 250 mm. In spite of this supposedly constant elevation of blood-pressure there was no evidence of hypertrophy or dilatation of the left ventricle. When first seen the patient had a bursting tension in the femoral artery that was consistent with the brachial measurement, but after rest in bed for four days with the use of trinitrin the brachial pressure was unchanged although the bursting tension in the femoral artery was much lowered. When the pressure was taken in the leg it was 150 although the brachial measurement remained at 250. A few days later under the continued use of trinitrin the arterial pressure in the brachial came down to 150. Evidently we were dealing with a regional hypertonus that must have been fairly constant although the aortic pressure could not have been persistently high. This, of course, did not prove that the patient had no organic disease of the heart or coronary arteries, but it did prove that there was not a constantly high aortic pressure which would have been assumed had the blood-pressure apparatus been unquestionably employed.

It is common to examine patients who have a maximum arterial pres-

sure of 180 and a minimum diastolic pressure between 90 and 100, with a heart-rate of 76 per minute. A few years later the same patient has a further elevation of the diastolic pressure, but the pulse-pressure will not be so large. Another patient may have a large pulse-pressure which in later years becomes smaller by a diminution of the maximum systolic pressure. How are we to explain the primary systolic rise of pressure? Are we dealing with a genuine hemic plethora? An increased systolic output of the heart? A hypertonus of the arterial branches? A sclerosis of the small arteries? All these factors must be taken under consideration. Of course, an elevation of the diastolic or minimum pressure means an increased peripheral resistance, but it is quite conceivable that there may be an increased peripheral resistance that would cause lessened yielding of the walls of the small arteries at the height of the heart's systole and still permit a descent nearly or quite to the originally normal diastolic pressure.

For the problem of heightened systolic pressure with a diastolic pressure that is not clearly elevated we have no ready solution. Some of these patients in subsequent years develop well-defined cardiovascular disease with hypertonus and others are found in later years with a sound cardiovascular system. In former years some of these doubtful vascular cases were described as vascular erythrim, a preliminary stage of arteriosclerosis. An increased cardiac output was suspected and suggested as the pathological physiology of the erythristic stage that preceded vascular rigidity. We have not arrived at a solution of these questions because a dependable method for estimating the cardiac output has not been evolved. When this has been accomplished we will be able to make a clear evaluation of peripheral resistance, hemic plethora and enlarged cardiac output. As diagnosis now stands we have only the pulse-pressure, the periphery of the ventricles, and the palpability of the diastolic systolic excursion of the two ventricles to guide us in our diagnosis and prognosis.

Alteration of Blood Flow.—Due to other causes than heart disease, there may be great alterations of blood flow that produce severe circulatory symptoms which may be misinterpreted as signs of heart disease. The most common is the increased minute volume flow in Graves' disease. The cause thus far is unknown, although it is commonly ascribed to "hyperthyroidism," a word that has achieved wide currency in medical writings with very few facts to justify its use. A mental concept may be false but unfortunately when adorned with a new word so much confusion arises between the word and the concept, that the false concept takes on the appearance of truth and joins the march of our scientific vocabulary which masquerades so much of the unknown as knowledge.

However, there is sufficient evidence to prove that there is an increased minute volume flow in the early stage of Graves' disease and unless recognized as such the symptoms are very likely to be misinterpreted as a purely functional nervous disorder of the heart. To compensate for the increased volume flow the heart enlarges its diastolic systolic excursion, the two ventricles are enlarged and both share in the precordial impulse. Consequently the cardiac impulse is very large and strong and carries with it an area of the anterior thoracic wall that is much larger than the

frontal projection of the heart. The area of cardiac impulse will therefore indicate the heart to be larger than percussion and the roentgen-ray both show it to be. When, however, the heart's area is decidedly increased the right auricle does not contribute to the enlargement. The atrio-ventricular circumference is not increased as in cardiectasis and the inferior aspect of the heart does not flatten the subcardial diaphragm as would the same degree of precordial enlargement with hypertrophy and dilatation. Therefore the diaphragm will not restrain the lateral movement of the inner portions of the costal borders as the enlarged heart otherwise does. This is very important because it serves to differentiate between a compensatory dilatation and hypertrophy with ectasis of the ventricles that occur in primary disease of the myocardium. Both conditions produce a globular enlargement of the heart, but compensatory dilatation does not flatten the subcardial diaphragm. This differentiation cannot be made with the skiagram because the nest of the heart and pericardium on the left lobe of the liver is opaque to the roentgen-ray.

Arterio-venous Fistula.—For similar reasons the functional enlargement of the heart in arterio-venous fistula may impose on the examiner as a primary myocardial disease. When the arterio-venous fistula is large enough to cause a compensatory dilatation from the increased volume flow through the heart it may sooner or later cease to adequately propel the increased blood-volume offered from the venous side and then a strong hepatic pulse develops which adds still further to the suggestion of a primary cardiac incompetence. But even under these extreme circumstances if the globular heart consists wholly of ventricular enlargement without dilatation of the right auricle the true significance of the cardiac dilatation will be recognized. I have seen 4 such arterio-venous fistulae. Three were in the femoral and 1 in the carotid-jugular location and none of them had dilatation of the right auricle or flattening of the subcardial diaphragm although in all 4 cases the same cardiac volume caused by primary heart disease would have shown marked enlargement of the heart in its ventral aspect.

These two sources of ventricular enlargement without auricular dilatation are mentioned because it is very important in the study of circulatory function to clearly determine which chambers are affected and also to determine if the chambers are equally or unequally affected. It is only in this way we can learn if one side is affected secondarily to disease of the other side of the heart and whether we are dealing with a disease that is located primarily in the vessels, in one ventricle, in the myocardium, in volume flow or merely in a disturbed innervation. Before we are justified in making a diagnosis of extracardial sources for disturbed cardiac function all these questions must be answered and as a rule the answer rests on careful and minute physical examination.

In recent years there have been such important mechanistic aids devised for diagnostic purposes that instead of being used as diagnostic auxiliaries they have been too often substituted for intelligent observation. This is a real danger, for instrumental exercise that is not guarded by adequate criticism leads to deterioration of an art, and there is no field of diagnosis where one must depend so much on intelligent observa-

tion and rest so little on instrumental devices as in differentiating between a *functional disability* and a *primary disease* of the heart.

Functional Abnormal Blood Distribution.—By this we mean that the cardiac output is adequate but that the several destinations of the aortic blood are not normally apportioned. The large splanchnic vessels maintain a very nicely balanced relation to the needs of the brain and extremities. If the large abdominal vascular bed loses its vasomotor resourcefulness, difficulty arises immediately if the horizontal is changed for the upright position. Impairment of this vasomotor response to change of posture may often be responsible for the complaints of some of our nervous patients and may also explain the relief obtained by wearing abdominal supports. If, when the upright posture is assumed, the splanchnic vessels do not vary their size, the brain will receive less than its needed portion of blood and a depressing sense of weakness follows that at first may seem to the examiner as an unreasonable complaint, but if the volume- and blood-pressure in the carotid and brachial arteries are observed when the patient is alternately horizontal and upright the weakness is readily explained. This is a rare complaint in *tabes dorsalis*, and in view of the frequent lesions of the nerve roots in this disease it is surprising that it does not occur oftener. The mechanism that underlies the symptom can be pictured by the description of a patient in the Lakeside Hospital.

The patient was a colored woman, aged fifty-four years, who had symptoms that strongly suggested pulmonary and mediastinal tuberculosis and syphilis of the dorsal spinal cord. Air hunger and cough were the symptoms that led her to seek hospital aid. On admission she had moderate emphysema with a low position of the borders of both lungs, but the total lung volume was not sufficiently increased to flatten the arch of the diaphragm so as to modify the inspiratory lateral excursions of the costal borders. There was pronounced dyspnoea with a vital capacity of only 900 cc. which promptly rose to 2500 cc. after 1 cc. of 1 to 1000 solution of epinephrine was given subcutaneously. A few days after admission while seated in a chair she was seized with severe pain along the third and fourth interspaces from the axillary line of the left side and extending over the precordial region. There was a distinct pleural "stitch," and tenderness on pressure over the painful area. Shortly afterward she expectorated a small amount of mucus stained with blood followed by a stormy attack of tachypnoea which attained a rate of 76 per minute. The respiratory excursions were very small and taken with the lungs in a moderately deep inspiratory phase. The heart-rate increased from 80 to 110 and the systolic pressure rose from 110 to 130 mm. Hg. The dyspnoea and tachypnoea suggested mediastinitis as a cause and the acute pleurisy added strongly to the suggestion that mediastinitis was responsible for the symptoms described. It was then discovered that when the patient sat or stood up she suffered severely from a feeling of weakness which she referred to the epigastrium. When lying down the carotid and femoral arteries were full and proportionately larger than the brachials and radials. When the patient stood erect the carotid artery grew much smaller but maintained nearly the same rate. The brachial blood-pressure was 130 when lying down and 110 when erect.

Further examination revealed hypersensitiveness to cold on the left side of the lower thorax and upper abdomen. The right ankle reflex was absent and over the left leg and foot there was impairment of both superficial and deep sensations. The response to the plantar scratch approximated the Babinski sign; the toes halted between flexion and extension. In the horizontal position this patient could do vigorous muscular exercises without exhaustion but she was unable to walk when she stood up. This description portrays vascular incompetence from a loss of pressor vasomotor response caused by a common organic disease of the spinal cord. The wonder is not that such symptoms could occur but rather why they are not more frequent. Pressor vasomotor responses in the splanchnic vessels are common occurrences under other conditions than tabes but in this disease are very rare in view of the fact that sensory crises so frequently characterize it. I do not recall a single instance of tabes in which regional vascular crisis could be assigned as a cause for the symptoms complained of by patients.

True *abdominal angina* with a critical rise in arterial pressure is occasionally found in patients with sclerosis of the splanchnic vessels. The patient complains of widely distributed abdominal pain that cannot be accurately located or limited. The abdomen is nowhere tender to pressure and the pain is not attended with gastro-intestinal symptoms. The only indication for a splanchnic vasomotor crises as a cause is the acute rise in arterial pressure which (with the pain) immediately subsides after the administration of vasomotor depressants like trinitrin or amyl nitrite.

Vasomotor crises limited to the arms occurred in one patient who had lung tuberculosis and mediastinitis. When these crises came on they caused no discomfort in the arms although both radial pulses entirely disappeared at the same time as the aortic pressure rose from 130 to 150 mm. The patient had extreme air hunger with great increase in the frequency and depth of respiration and with these paroxysms of air hunger the pulse at the wrists was not palpable. It was the want of radial pulsations that led the patient to seek hospital aid for supposed circulatory failure, but there was no evidence of impairment of the volume flow of blood through the heart during the paroxysms.

Many years ago I was consulted by a man, aged fifty years, who complained of vascular crises in the left arm that were proved by subsequent events to have been caused by cerebral syphilis. At any rate after vigorous antisyphilitic treatment the brachial and cerebral symptoms subsided. The brachial symptoms could be brought on at will when the patient would lie for a few minutes on his left side with the arm under him. The left arm then became livid, the veins from the hand as high as the shoulder-joint were distended under high pressure. The total volume of the whole upper extremity was increased and the arterial pulse at the wrist was plainly palpable although somewhat obscured by the acute swelling of the surrounding tissues. The appearances on the arm could be explained only by a paroxysmal constriction of all the effluent large veins of the upper extremity with a persisting flow of affluent arterial blood. The vascular spasm could always be relieved by traction on the arm when held at a right angle to the trunk. After vigorous pulling on

the arm for about fifteen seconds the tightly distended veins collapsed, the pain ceased and the arm resumed its normal appearance. The whole procedure looked as though a ligature had been applied around the shoulder-joint sufficiently tight to shut off completely all the effluent venous flow, but still to permit the affluent arterial blood to flow into the arm. Of all the cases of regional vasomotor spasm that have come under my observation this is the only one that could be interpreted as a vasomotor constriction of trunk veins.

Spasm of the Retinal Arteries.—Regional arterial constriction in the retina affords the only opportunity to see plainly the constricted artery for its full length. Without any assignable cause this rare phenomenon begins by obscuration of vision. The patient complains of seeing everything as through a dense mist. The impairment of sight persisted in one of my patients for a whole day and then with returning vision intense photophobia lasted for half a day before normal vision returned. During the period of blindness the retinal arteries could be seen as the so-called silver-wire arteries with their lumina reduced to a very minute calibre. When we consider the neuro-muscular provision for the arteries and veins and the variable capillary blood flow under different influences it seems strange that in disturbed emotional states and in organic nervous diseases we do not oftener see severe regional disturbances in blood flow.

In the writer's experience the end-results of anterior poliomyelitis have shown more evidence of disturbed blood flow in the extremities than in all other nervous diseases. There has always been lessened flow through the capillaries of the skin. In some instances there have been mingled livid and pale areas that were cold, and in others the extremity was uniformly pale and cold. How much the splanchnic blood flow may be altered as a result of organic disease of the cord is beyond our diagnostic resources, for it is only the gross effects on aortic pressure that enable us to detect them, but it is quite possible that many digestive symptoms may be due purely to functional disturbances caused by impaired blood flow in the alimentary tract and in the liver and pancreas.

Arrhythmia, Bradycardia and Tachycardia.—The electrocardiograph has added greatly to the accuracy of the interpretation of the auriculo-ventricular mechanism but it is an error to assume that altered transmission of the intracardiac contraction wave is always due to intracardiac disease. A slow ventricular with rapid auricular rate may result from disturbed gastric function and from bulbar diseases. In this chapter a patient has been described who had many attacks of paroxysmal tachycardia associated with functional digestive symptoms and the same patient had one attack of paroxysmal heart-block in which the ventricular rate was only 15 per minute and very irregular with very rapid pulsations in the distended right bulbus venosus. In all the attacks of tachycardia as well as in the single attack of heart-block the normal rate and rhythm returned after the eructation of a large amount of gas from the stomach. This patient has been under observation for twenty-seven years and has been quite free from any cardiac symptoms for nearly twenty years. The patient is a woman now aged sixty years, and has had excellent health ever since the paroxysms of tachycardia ceased.

Auricular fibrillation may occur in patients with digestive symptoms that bear no other interpretation than functional neurosis. The auriculo-ventricular mechanism is identical with that found in association with organic heart disease; but the patients have a normal heart mechanism in the intervals and live for so many years without the development of any signs of heart disease that we are bound to regard the transient fibrillation as a symptom of a functional nervous disorder.

There is also very good evidence for the extra-cardial origin of heart-block and Stokes-Adams syndrome due to organic bulbar disease. In my contribution to the first edition of this work twenty years ago a case of Stokes-Adams disease was described in which there was a 3 to 1 auriculo-ventricular rate, but the greatest discomfort to the patient was slumber apnœa with waking hyperpnœa that prohibited sleep until the early morning hours. This symptom from a diseased respiratory centre was not traceable to circulatory failure or retention of body fluids and the heart-block and slumber apnœa ceased simultaneously on the fourteenth day of a vigorous mercurial therapy. It seems very improbable that if the heart-block had been due to syphilitic disease of the heart and the slumber apnœa to syphilitic bulbar disease the two symptoms would have ceased on the same day, whereas if both symptoms were due to bulbar meningo-angiitis they would very probably disappear at the same time.

The results gained thus far are so uncertain about the nature and course of afferent and efferent impulses along paths that include the sympathetic and parasympathetic nerves that we are left to contemplate the symptoms with inferential evidence only as to the source and nature of the stimuli that produce them. If in the presence of mediastinitis we have dyspnœa, tachypnœa, bradycardia, heart-block, or spasm of the brachial arteries, there is a very suggestive source for the symptoms, and if disturbances in rate and rhythm of the heart are altered by surgical procedures and inflammatory processes in the pelvis there is good contributory evidence to indicate reflex nervous action as the cause of the cardiac symptoms, but the exact courses of the afferent and of the efferent impulses remain unsolved.

If, as I have seen, a patient has paroxysmal tachycardia for a period of seven years and during that time is constantly harassed with the fear of organic heart disease and then by some evidence the patient is convinced there is no danger of heart disease and from that moment the attacks do not recur for twenty years there is excellent reason for believing the tachycardia was due either directly or remotely to cerebral stimuli.

Disorders in the Stomach.—The most frequent source for cardiac arrhythmia secondary to other disorders is the sinus arrhythmia associated with the complaint of "gas in the stomach." This complaint by patients is due usually to a disturbed gradient in gastric peristalsis and rarely to a real increase in the amount of gas in the stomach. Frequently it is difficult to determine whether the arrhythmia and gastric symptoms are due to a common cause, or the cardiac arrhythmia is caused by a reflex action due to afferent impulses from the stomach. There is, however, good evidence to indicate that the heart's rhythm can be much disturbed by distention of the gastric wall under pressure. Prior to the use

of the roentgen-ray for the study of gastric motility it was a common practice to give patients Seidlitz powders with the acid and alkaline portions separated. The resulting ebullition of gas enabled one to locate the borders of the stomach. On one such occasion the patient had a diffuse carcinoma of the stomach that greatly reduced the extensibility of the gastric walls. Consequently, the gas being evolved within a cavity with rigid walls, the intra-gastric pressure must have risen to a considerable height. The results were quite alarming, for the patient suffered great pain and the heart took on a very slow rate with arrhythmia. During this procedure the patient was seated on the edge of the bed. The whole process did not last longer than half a minute. The bulbus venosus was distended and pulsated very rapidly while the heart impulses occurred irregularly and with a rate that was as low as 20 per minute. The demonstrable evidence strongly suggested a functional heart-block. Such symptoms must certainly have been caused by excitation near the cardia and not from upward displacement of the diaphragm. If the latter process could cause such cardiac disturbances they should commonly occur in other diseases attended with abdominal distention.

Another clinical experience strongly suggests reflex vagus affects as a cause for cardiac arrhythmia. A woman, aged forty years, who had been much disturbed nervously and who had lost much sleep developed a great deal of gastric distress attended with sour eructations. She then observed that every time she swallowed her heart intermitted and to prevent this distressing symptom she spent the entire night lying on her right side with a towel tucked under her head to catch the flow of saliva she dared not swallow. A stomach tube was passed for gastric lavage and caused no cardiac intermissions. If there was as much as a pint of water in the stomach, extra systoles occurred when the patient turned on her back or left side. Apparently the arrhythmia was produced from stimuli in the œsophagus and from the cardiac end of the stomach. To produce such symptoms there must have been a low threshold for the vagus reflex. The gastric disturbance alone could not have been responsible for if this were true we should often see this result in persons with carcinoma and ulcer and other organic diseases of the stomach.

Not only do we see these astonishing cardiac symptoms accompany functional gastric disturbances, but there is also a clear relation between some organic diseases of the heart and gastric function. This relation is equally intimate and inexplicable in some cases of syphilitic aortitis and myocardial disease. The patients have much precordial pain after eating, although the amount of food taken may be very small. With an empty stomach they can exercise with considerable freedom; after a small meal they are compelled to remain absolutely at rest to escape the severe pain that would follow moderate walking. This does not explain our problem but it does emphasize the very intimate nervous relation that exists between the cardiac and gastric functions. This is a fact plainly apparent to the patient, but often ignored by the physician. In nervous patients gastric and cardiac symptoms occur so often at the same time that it is impossible to know if the cardiac come with the gastric symptoms from a common cause or originate secondarily to the gastric disturbance.

Auricular Fibrillation.—A man who for years has suffered from stomach symptoms (that have never been satisfactorily explained) on several occasions developed auricular fibrillation. During the attacks neither ventricle was enlarged, but the right auricle was enlarged to the right of the sternum. These attacks accompanied functional disturbances in the stomach motility and ceased without medication just as suddenly as they began. Thus far the heart has shown no evidences of disease and although for several years these attacks of auricular fibrillation have recurred at irregular intervals the heart has apparently lost none of its reserve energy.

ANGINA PECTORIS

As the writer's experience with angina pectoris presents itself there are three facts with which to reckon, namely, pain, arterial spasm, and disease of the coronary arteries. Pain is always present. Arterial spasm frequently attends the pain but may be absent, and in my experience disease of the coronary arteries has always been found in every case that was subjected to a thorough postmortem examination. In fact the problem to my mind resolves itself into a question as to how disease of the coronary arteries may account for pain and arterial spasm.

As patients with angina pectoris are commonly seen the pain is apparently a symptom of arterial spasm, but how pain can be produced by a paroxysmal hypertonus of the aortic branches is not explicable unless hypertonus of the aortic branches is attended with some unusual behavior of the coronary arteries. Apparently a sharp rise of the endaortic pressure produces cardiac pain only when it is attended with an abnormal response in the coronary arteries.

It is not unusual to see transient rises of pressure in the aortic pressure without cardiac pain, but in a patient with general arteriosclerosis a typical attack of angina with arterial spasm can be produced by the use of epinephrine and the pain and spasm are promptly relieved by nitroglycerine. The whole play of symptoms is quite like the attack and relief so commonly seen when patients spontaneously develop spasm and pain and both are relieved by nitroglycerine.

The experiment was done on a man, aged fifty years, who had cardiac decompensation with cardio-arterial sclerosis. There was cardiac enlargement and general anasarca with a genuine failure of blood hydraulics although the pulse-pressure was within normal limits and the maximum pressure was not above 130 mm. Although the diastolic pressure was not high the artery did not collapse between the heart beats but apparently contained a large amount of blood that received insufficient propulsion from a failing myocardium. One minim of 1 to 1000 solution of epinephrine in 1 cc. of physiological salt solution was injected into an arm vein. By the time the piston of the syringe was driven home, the radial artery contracted so strongly that the pulse was almost imperceptible and the patient had violent pain over the lower half of the sternum and over the median aspect of the middle of both arms. The pain was instantly relieved when several drops of 1 per cent. nitroglycerine solution were put on the tongue. The attack thus artificially produced was exactly

like those attacks which come on spontaneously, but it must not be forgotten that the patient had general arteriosclerosis and also, in all probability, sclerosis of his coronary arteries. It is therefore not justifiable to assume that the attack was due purely to a rise of endaoctic pressures, for patients with arteriosclerosis commonly have paroxysms of arterial hypertonus without pain or discomfort of any kind. Certainly, a rise of endaoctic pressure alone will not account for precordial pain although patients who have only a small segment of one coronary artery diseased may have arterial hypertonus with their angina and the pain ceases when nitroglycerine is given and the hypertonus subsides. The same patient, however, may have other attacks of angina without myocardial infarction and without rise of arterial pressure, but in such attacks nitroglycerine gives no relief from pain. Why one attack is attended with hypertonus and another is not cannot be explained. In either case the mechanism which produces the pain is not understood. However, in the presence of coronary disease we imagine that transient ischemia of the heart muscle produces pain just as intermittent claudication occurs with disease of the femoral arterial supply or intestinal colic attends disease of the mesenteric arteries.

There is, however, some difference between angina accompanied by arterial hypertonus and the angina without hypertonus. The patient who has angina with arterial hypertonus is one who corresponds to the traditional symptom of annihilation and locates his pain in the mid-sternal region over the heart and in the arms and forearms. He is "fixed to the spot" and fears to move, whereas the patient who has angina without hypertonus may locate his pain over the precordial region to the left of the sternum or elsewhere than over the heart. It is not uncommon to see these patients walk about the room as they complain of their pain. They are not "fixed to the spot" like the angina patient with arterial hypertonus.

Pain.—Neither the mechanism of production nor the paths of transmission of cardiac pain are definitely known. Cardiac pain may be severe and persist for many weeks without being attended or followed by other severe symptoms. Mitral stenosis is sometimes attended with severe precordial and subscapular pain when the rate and rhythm of the heart and the volume flow fail to indicate a severe heart lesion. One patient of this kind was first seen twenty-seven years ago and is still living with a heart that permits the patient to lead an active life. Cardiectasis seems at times to be a source for pain just as stretching Glisson's capsule causes pain from stasis in the hepatic veins. Functional ischemia of the myocardium causes pain when the physical work of a patient exceeds the amount that can be supported by the lessened volume flow through a stenosed coronary artery. But none of these sources for heart pain produce attacks which are identical with angina pectoris.

When a patient has violent pain which he locates by placing the ends of his approximated fingers over the lower end of the sternum as if he wished to indicate a narrow painful strip in the middle of his thorax and at the same time complains of pain over the inner aspect of either or both arms, and palpation of the arteries indicates hypertonus, the

diagnosis is simple enough. The patient is given nitroglycerine or amyl nitrite, whereupon vasomotor relaxation follows and the pain is relieved. Such cases offer no diagnostic difficulties but the problem is very different when the only symptom is pain over the precordial area to the left of the sternum. The heart area, the blood-pressure and the rate and rhythm of the heart may be normal. The auriculo-ventricular mechanism conforms to the normal ideal and the pain does not seem to sustain a constant relation to exercise. One day the patient may exercise without the penalty of pain and another day the least exercise causes violent pain. In the intervals the heart and circulation fail to reveal the least indication of cardiac disease and even when the pain is severe all other symptoms are wanting. Instead of remaining fixed to one spot, like the patient with mid-sternal pain and arterial spasm, the patient wanders about the room or may move about in a manner that suggests there can be no serious impairment of the heart's functional ability. One such patient, who at autopsy was found to have extensive sclerosis of the coronary arteries, was accustomed to exercise vigorously to "work off his pain" when the attacks began. In later years he would stand erect with his head in hyperextension and the cervical muscles strongly contracted which was the only device he could employ to lessen his pain.

In some cases of coronary sclerosis with angina the pain is not located in the cardiac region and is not associated with any other symptom that suggests a cardiac source for the pain. A man whom I observed for two years before his death, due to extensive sclerosis of the coronary arteries, complained of paroxysms of severe pain over the left mastoid region. Exercise did not bring on the attacks and indeed the final attack was not attended with precordial pain, but with pain in the left hypochondrium that suggested a return of renal colic due to calculi which the patient had had several times in former years.

Pathological Lesions of the Heart and Angina.—Great caution must be exercised in excluding organic disease of the heart because no evidence can be found to indicate any change in the heart volume, rate, rhythm, arterial pressure or auriculo-ventricular mechanism. The most careful search for such evidence may be futile, but a postmortem examination may reveal a severe lesion of the heart muscle.

A man, aged fifty years, who had endured angina for fifteen years afforded such an example. For thirteen years he pursued his vocation as a traveling salesman although harrassed much of the time with his pain. For the last two years of his life the pain occurred so often he was compelled to give up his work. When seen at Lakeside Hospital the heart volume, rate and rhythm and the blood-pressure and electrocardiogram revealed no evidence of organic disease of the heart, aorta or arterial system. The history indicated that there was not a constant relation between the precordial pain and exercise. In the course of fifteen years this man visited many diagnosticians who, in the early years of his disease, unhesitatingly diagnosed angina pectoris, but as time went on the diagnosis became uncertain and finally he was assured by several competent examiners that his pain could not be due to an organic disease of his heart. This seemed to be an instance in which sympathectomy would

be justifiable. The night before the operation was to have been performed he died suddenly and the autopsy revealed extensive disease of the heart muscle in both ventricles; both coronary arteries were sclerosed throughout their entire lengths.

Another patient, a woman, aged fifty-five years, had repeated attacks for seventeen years when she committed suicide. No autopsy was performed but physical examination revealed no evidence of organic disease of the heart or aorta although there was marked arterial hypertonus with the attacks of pain, and at frequent intervals the arterial pressure would be as high as 250 mm. When there was no pain, the patient sometimes had arterial hypertonus and at other times a normal arterial pressure of 150. It seems very improbable that an arterial pressure of 250 could have persisted much of the long period of seventeen years and not produce some evidence of hypertrophy or dilatation of the left ventricle.

Vasomotor angina and angina from abuse of tobacco may be due to a transient disturbance in the arterial supply to the myocardium which has no grave significance and the patients may have no recurrence of the attacks, but to prove such a statement is extremely difficult. A few years of freedom from attacks does not prove the absence of a grave pathological lesion and the want of clinical evidence for disease of the heart does not prove that the heart is anatomically sound. In medical literature many cases are described that were not under observation very long and many cases of fatal angina pectoris have been interpreted as having no anatomical lesion because none could be demonstrated in life.

As our experience with angina grows and we find patients leading comfortable lives for an interval of several years who then die suddenly from coronary disease and furthermore when we find patients who die from angina due to myocardial disease which may last fifteen years without revealing any clinical sign of heart disease, we must be very cautious in assuming there can be no heart lesion merely because clinical evidence fails to indicate its presence.

Medical Treatment.—When the attacks of angina are based on paroxysms of arterial hypertonus the pain can be relieved by nitrites, but they are not effective if the paroxysms of pain are unattended with arterial hypertonus. The nitrites, of course, never offer more than symptomatic relief; they do not protect against recurrences of pain or progress of the underlying disease.

When the basic anatomical disease is cardiovascular syphilis in which the coronary arteries are involved, antisyphilitic treatment may influence the anatomical disease which causes the symptom of angina, but in my experience the syphilitic patients who have been relieved by treatment did not have attacks of pain which come with paroxysms of arterial hypertonus when at rest. These patients presented the picture of functional ischemia of the heart. There was apparently inadequate blood flow through the coronary arteries to permit physical exercise. The attacks were analogous to intermittent claudication in disease of the femoral arteries. Strictly speaking the patients were cured of functional ischemia of the heart by improvement of the coronary arterial lumen, but they

were not cured of angina pectoris that was concurrent with arterial hypertonus and that occurred independently of exercise. Besides caution in exercise the patient should not put, at one time, a large bulk of either solid or liquid food in the stomach, and constipation and flatulence should be avoided. All precautions should be observed which protect the patient against increase of intra-abdominal pressure.

Surgical Treatment.—A variety of operative procedures have been devised with the hope of giving protection against the symptoms of angina either by interrupting the afferent impulse that conveys the experience of pain or by interrupting either the afferent or efferent impulse in a reflex arc that furnishes the anatomical basis for the physiological mechanism that produces the experience of pain. There are three distinct and separate procedures, any one of which if successful in their aim would stop the pain. From the reports thus far there is not sufficient evidence to indicate which one of the three procedures was accomplished in any of the supposedly successful cases. Furthermore, the paths of the sympathetic afferent impulses from the heart are only vaguely and uncertainly known. The entire cervical sympathetic system is believed by the best investigators, Langley¹ and Ranson,² to be purely efferent. If section of this system cures angina it must do so by interrupting the efferent impulse. If improvement follows removal of the stellate ganglia it may be due to interruption either of the afferent sensory or the efferent motor sympathetic impulses. From the case reports there can be no judgment formed as to what may have been the relation of failures and successes to arterial hypertonus, which is an important element that has been neglected in all the surgical reports. Section of the depressor branch of the vagus has no physiological or anatomical support and rests purely on empirical grounds. Paravertebral injections of alcohol in the vicinity of the dorsal nerve roots with the hope of anesthetizing the sympathetic ganglia have been advocated and supported by claims of success.³

It seems very strange that all these different methods of attack should be attended with equally good results. This fact alone should make one very cautious in accepting any of them. In these different procedures have any real value it seems that our present knowledge of the anatomy and physiology of the heart's innervation will have to be fashioned anew.

Critical surgical experience as interpreted by Cutler⁴ leaves the whole question in great doubt. Were all the failures reported the proportion of successes to failures would certainly be much smaller than the present statistics of six successes to four failures.

STOKES-ADAMS SYNDROME

The Stokes-Adams syndrome is applied to certain symptoms and not to a definite pathological process. It is not synonymous with heart-block. The causes which give rise to the symptoms may produce their manifes-

¹ Langley, J. W.: In textbook by E. A. Schafer, ii, p. 616.

² Ranson, S. W.: *Anatomy of the Nervous System*, W. B. Saunders, 1923.

³ Swetlow and Schwartz: *Jour. Am. Med. Assn.*, 1926, **86**, 1639.

⁴ Cutler, E.: *Jour. Am. Med. Assn.*, 1926, **86**, 1972.

tations through irritation of the medulla, upper cervical cord, and vagus trunk, or there may be in addition to the purely nervous influences some lesion in the myocardium which contributes to the slow heart rate and arrhythmia commonly present. But bradycardia is not responsible for the cerebral symptoms which accompany the paroxysms. The symptoms vary with the disease of which they may happen to be a manifestation. The clinical picture of pressure on the medulla or upper cervical cord would differ widely from that of sclerosis of the brain arterial supply with chronic interstitial nephritis and sclerosis of the coronary arteries with secondary disease of the myocardium.

The symptoms are both cerebral and cardiac in origin, although bradycardia and arrhythmia are the most striking features in many cases. Nervous influences may cause a bradycardia or rather slow pulse in several ways. There may be negative chronotropic or negative bathmotropic influences applied to the supposed seat of origin of cardiac rhythm, namely, at the junction of the veins with the auricles, or on account of negative dromotropic influences at the atrioventricular junction heart-block may result, and although the auricle continues a normal or rapid rate, the systolic wave is blocked at the atrioventricular junction and the ventricle does not share in the systole. This procedure can be distinctly seen with the fluoroscope. The contractions of the right auricle can be clearly seen and during the block the ventricle is seen to gradually enlarge, and with a complete heart cycle the systole of the ventricle can be clearly seen to succeed the systole of the auricle. So we may have a bradycardia from purely nervous influences which involves auricles and ventricles, or a bradycardia which involves the ventricle only. In both conditions of course there is a slow pulse. The real problem, so far as the heart is concerned, is to determine whether we are dealing with a genuine bradycardia which involves both auricles and ventricles, or heart-block, in which the rhythm of the auricles is maintained, but the ventricle fails to follow. The other problem to determine is where the nervous stimuli arise, in the brain, medulla, cervical cord or vagi, and whether these stimuli arise from disturbances in the vascular supply to these parts or from pressure or intrinsic disease of these structures.

By far the most common association of the Stokes-Adams syndrome is with arterial sclerosis, and in this affection the three organs which suffer mostly from secondary effects are the heart, brain, and kidney. Vascular crises in different parts of the arterial supply are common in this disease. Besides the results of vascular crisis in the arterial supply to the brain there may be many symptoms constantly present. Sclerosis of the coronary arteries commonly results in secondary diseases of the myocardium, which may cause a genuine bradycardia and also heart-block. We have the pathological conditions for bradycardia and heart-block constantly present, and also the necessary conditions in the arterial supply to the brain which produce paroxysmal attacks of bradycardia and heart-block. The other symptoms from the brain are very commonly seen in persons with sclerosis of the cerebral arteries. His recognized the significance of these symptoms in relation to the myogenic theory

of the cardiac rhythm (as conceived by Gaskell) and also the rôle of "Gaskell's bridge" in the embryology and physiology of the heart as described by Stanley Kent.

Symptoms.—The patients are usually past middle life and present signs of arterial sclerosis. Bradycardia and arrhythmia are constantly present. The heart rate is commonly 40 or thereabouts, but during the paroxysms the rate becomes slower. In one fatal case described by Huchard the rate was as low as 2 to the minute. The pulse may be very irregular. There is not a constant relation between the cerebral symptoms and degree of bradycardia and there is no reason to regard the brain symptoms as secondary to the bradycardia. A heart rate of 30 may accompany an apoplectic or epileptic seizure, and the same rate with perfect rhythm has been seen in a neurasthenic man who complained chiefly of symptoms due to dyspepsia. Under paroxysmal tachycardia one instance of sudden transition from paroxysmal tachycardia to paroxysmal bradycardia and arrhythmia with a heart-rate of only 16 to the minute has been noted. There were all the signs of heart-block one sees in the Stokes-Adams syndrome. Yet there was not the slightest suggestion of any cerebral symptoms. There is very strong evidence that the bradycardia of the paroxysms has its origin in negative chronotropic impulses from the cardiac nerve supply either in the medulla or in its path from the medulla to the heart.

The *cerebral* signs are due to crises in the vascular supply to the brain and medulla. These may vary greatly in character with the severity of the attack and the parts of the encephalon chiefly implicated. The attack may be merely syncope, epileptic, or apoplectic in character, with stertorous breathing or even Cheyne-Stokes respiration, but at autopsy no pathological signs are found in the brain tissue which can be associated with the paroxysm. This is quite conceivable if we think of the vascular spasm and its results as seen in the retina, extremities, and intestines. Both irritation and anemia of the medulla cause slowing of the pulse. Halberton's case, one of the earliest of this kind described and referred to by all writers on the subject, was that of a man who developed the symptoms three years after a fall from his horse in which he struck on his head. The autopsy revealed narrowing and deformity of the foramen magnum, and thickening of the dura mater which was sufficient to compress the cervical cord and medulla. Other cases of Stokes-Adams syndrome have been observed which have come to autopsy and skilled pathologists were unable to demonstrate any lesion in the medulla or in the cardiovascular system.

The whole symptom complex may arise from irritation of the *vagus* trunk. Probably the best evidence is to be found in Tanhoffer's¹ description of his experience with a pupil who was making some experiments on his own vagi for his professor's benefit. This student compressed with his left index finger and left thumb respectively his right and left vagi. Tanhoffer observed, while making sphygmographic tracings of the pulse, that his pupil did not respond to a question. On looking

¹ *Centralblatt f. med. Wissenschaft*, 1875, p. 403.

at his face, Tanhoffer observed his eyes had a glassy stare, and the left arm was rigidly contracted, with the finger and thumb pressing at the throat. The student had lost consciousness. Tanhoffer pulled the hand away from his throat and observed the pulse had ceased, the sphygmogram showing no tracing of the pulse for 67 seconds; then the pulse steadily rose in frequency. The student was unconscious for several minutes, and when consciousness returned he was dizzy and nauseated.

The physical signs over the heart, besides the bradycardia and arrhythmia, vary with the manner of heart-block or bradycardia. In instances of heart-block one may count the pulsations in the external jugular vein, as the veins of the neck under such conditions are greatly dilated. Under such conditions there can be seen two or more distinct pulsations in the veins for every pulsation in the artery. When the tricuspid valve is sound the venous pulses are due to the contraction of the auricle and can be seen to precede the carotid pulse in a complete cardiac cycle, and when the block at the auriculoventricular bridge occurs a pulse is visible in the jugular vein which marks the systole of the auricle.

The ventricles manifest some signs during the blocked systole. Although no pulsation occurs, one may hear a very faint sound over the ventricles. This is probably due to the closure of the atrioventricular valves which marks the termination of the auricular systole. At other cycles there may be an impulse over the ventricle due to an extrasystole which originates from the bridge and is not sufficient to produce a pulse, or, as Huchard suggests, such pulsations are due to distention of the ventricles from the auricular wave. This point can be determined only by an analysis of the comparative tracings of the venous and arterial pulses and cardiac impulses.

In one patient with a typical Stokes-Adams syndrome a marked improvement followed vigorous antisyphilitic therapy with both mercurials and iodide of potash. After this improvement, the heart rate remained at 60 to 70 per minute unless the patient exercised; then the heart rate became slow as before. The fainting, clonic convulsions, recovery from heart-block under antisyphilitic treatment, and subsequent slowing of the heart rate with exercise, all lure us to the ready conclusion that the heart-block was due to syphilitic disease of the bundle of His. But there were other features which serve to throw doubt on this explanation. The patient had sclerosis in all the accessible arterial distributions. During five consecutive months in which heart-block persisted, the patient dared not fall into a deep sleep. Whenever he went soundly to sleep automatic respiration ceased. If he was permitted to lie in this state of apnoea until he awakened spontaneously, he awoke with air hunger which was very distressing. The heart rate was not in any way implicated in this procedure.

During the greater part of the night the nurse awakened him promptly when respiration ceased. This procedure prevented the patient getting any sleep until the early morning hours, when he would finally fall into a light sleep which did not interfere with automatic respiration. After this prolonged siege with heart-block and slumber apnoea which lasted five months, his pulse was observed one morning to have attained a rhythmic

and regular rate of 60 per minute. From that time on he could sleep soundly through the night without any respiratory disturbance. The manner of recovery here does not offer any respiratory proof that the slumber apnœa and heart-block were both due to bulbar disease from sclerosis of the basilar arteries, but we know a definite relation exists between slumber apnœa and sclerosis of the cerebral arteries and we know of no causal relation between bradycardia and slumber apnœa. Such a case suggests the need of careful histological studies of the bulbar nuclei in cases of Stokes-Adams syndrome.

Disease of the bundle of His no doubt explains some cases of heart-block, but it is improbable that it will explain all cases any more than myocardial disease will explain all other changes in rate and rhythm of the heart-beat. There is another significant fact relative to this point, viz., the bulbar origin of the Stokes-Adams syndrome. Some cases have been reported in which the paroxysms of bradycardia and accompanying brain symptoms could be avoided by inverting the body. If measures which increase the blood supply to the brain will stop the paroxysms of Stokes-Adams disease, it seems reasonable to assume that bulbar anemia (in some cases at least) causes the heart-block.

Prognosis.—This is grave in any case of Stokes-Adams disease, though a prognosis for a short duration of life is not invariably justifiable. The course may be chronic but there is always the chance of sudden death. Frequent attacks and prolonged syncope are grave signs. In 1904 the writer, with S. J. Webster, saw a man aged seventy years, who had his first attack of convulsions when sixty-three years of age. Subsequently there were two more attacks. When serving as a soldier it was observed that he had a normal heart rate of 40, which rose to 50 under excitement. His health remained good until the attack seven years ago. He had a much enlarged heart, marked arterial sclerosis, and dilated and pulsating jugular veins. The carotid artery showed 36 pulsations to the minute. The jugular vein showed 72 centrifugal pulses to the minute and these were equidistant; so they were pulses from two distinct cardiac cycles, one of which was blocked and the other transmitted to the ventricle. A few months later Dr. Webster found the precordial area had increased in size, the distress and dyspnœa had increased, and there were three venous pulses for each arterial pulse. In the summer of 1907 the writer found him very much better. The venous pulses had entirely disappeared; the area of cardiac dulness had diminished, and the pulse rate was rhythmic, 76 per minute, and the arterial tension was markedly increased.

Treatment.—Besides the treatment of the underlying cause, such as syphilis, arterial sclerosis, and brain affection, the only specifics for the symptoms are: to put the head low or invert the body to counteract the anemia of the brain, which is supposed to be the cause of the symptoms, and to employ atropine to diminish the inhibitory tone of the vagus termination. Atropine is of service when the bradycardia is not due to heart-block or affections of the myocardium itself. In heart-block, Erlanger¹ has shown that atropine increases the rate of the auricle and

¹ *Journal of Experimental Medicine*, vol. 7, No. 4, and vol. 8, No. 1.

not the rate of the ventricle. Dehio has shown the efficacy of atropine in increasing the heart rate when the vagus inhibitory tone is increased, and the failure to give relief when bradycardia is due to disease of the myocardium; but his conclusions should not be rigidly adhered to in treatment, because benefit in myocardial cases may be got by diminishing the normal negative dromotropic influence of the vagus nerve or vagus nucleus. Epinephrine subcutaneously (M 10 to 15, 0.6 to 1.0, cc. of a 1 to 1000 solution) and barium chloride (gr. $\frac{1}{2}$, Gm. 0.03) by mouth four times daily have been found to benefit the syncopal attacks in some patients.

Syphilis must not be forgotten in treating any case of Stokes-Adams syndrome. Syphilitic myocarditis involving the bundle of His has been proved in several cases at autopsy. Syphilitic arteritis of the cerebral arteries may also be a cause. Not only iodide of potash, but mercury in sufficient doses must be used, for the chronic arteritis of syphilis responds to mercury when it is unaffected by iodide of potash, although the primary infection may have occurred many years before.

CHAPTER XXI

CONGENITAL CARDIAC DISEASE

BY MAUDE E. ABBOTT, M.D.

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PART I

GENERAL CONSIDERATIONS

Definition.—Congenital cardiac disease may be defined as that condition in which, through arrest of development or disease occurring in intra-uterine life, alterations in the anatomical structure of the heart or

great vessels exist, leading to irregularities in the circulation, which set up conditions of cardio-vascular strain, and frequently interfere with oxygenation of the blood in the arterial or capillary stream. In the latter event it is commonly associated with cyanosis and clubbing, and constitutes in extreme cases the *morbus caruleus* of the older writers.

THE DEVELOPMENT OF THE HEART

It is impossible to approach this subject intelligently without a certain preliminary knowledge of the development of the mammalian heart. A brief statement, referring especially to the development of the septa, the involution of the bulbus cordis, sinus venosus and primitive aortic arches, is therefore necessary here. For fuller details the reader is referred to the fundamental studies of His,¹ Born,² Tandler,³ Mönckeberg,⁴ Mall,⁵ Fraser,⁶ Waterston,⁷ Spitzer⁸ and Keith.

The mammalian heart is formed originally of two straight tubes placed independently on either side of the body, which merge together as the ventral cleft closes in and finally fuse, the septum thus formed becoming entirely obliterated before the permanent interventricular septum begins to appear. Meanwhile a twisting of the heart upon its long axis occurs, and it becomes no longer symmetrical, but S-shaped, with the ventricular portion bent forward and downward and the auricular part upward and backward. It now consists of two chambers, a single ventricle forming its anterior and lower part with its bulbus cordis passing upward and to the left and *giving off the aortic trunk from its right upper angle*, and a single auricle with its sinus venosus lying behind and to the left. At this stage it resembles the two-chambered heart of the fish, and is especially interesting in regard to the formation of the bulbus cordis.

The auricle next shifts upward, coming to lie above the ventricle, and its auricular appendages develop enormously, pouching forward on either side of the bulbus (Fig. 39). The atrial canal, in which are developing the endocardial cushions which are to separate the two venous ostia, has become elongated and still opens into the common ventricle entirely on the left side. The sinus venosus is now a separate cavity opening into the auricle on its right wall posteriorly through a narrow cleft, the edges of which project into the auricle as the *valvulae venosae dextra et sinistra*. At its upper border it is elongated laterally into the two sinus horns which receive the two superior venae cavæ, while a single short trunk, the inferior cava, enters it below.

The Bulbus Cordis.—This name is given to a transitory portion of the embryonic heart leading from the right end of the common ventricle to

¹ *Beiträge zur Anatomie des menschlichen Herzens*, Leipzig, 1886.

² *Beiträge zur Entwicklung des Säugethierherzens*, *Arch. f. mikr. Anat.*, 1889, vol. 33, 284.

³ Keibel and Mall: *Human Embryology*, 1912, 2, 534.

⁴ *Atlas der Herzmissbildungen*, Jena, 1912; also *Verhandl. d. deutsch. path. Gesellsch.*, Marburg, 1913, 16, 228.

⁵ *Am. Jour. Anat.*, 1913, 14, 249.

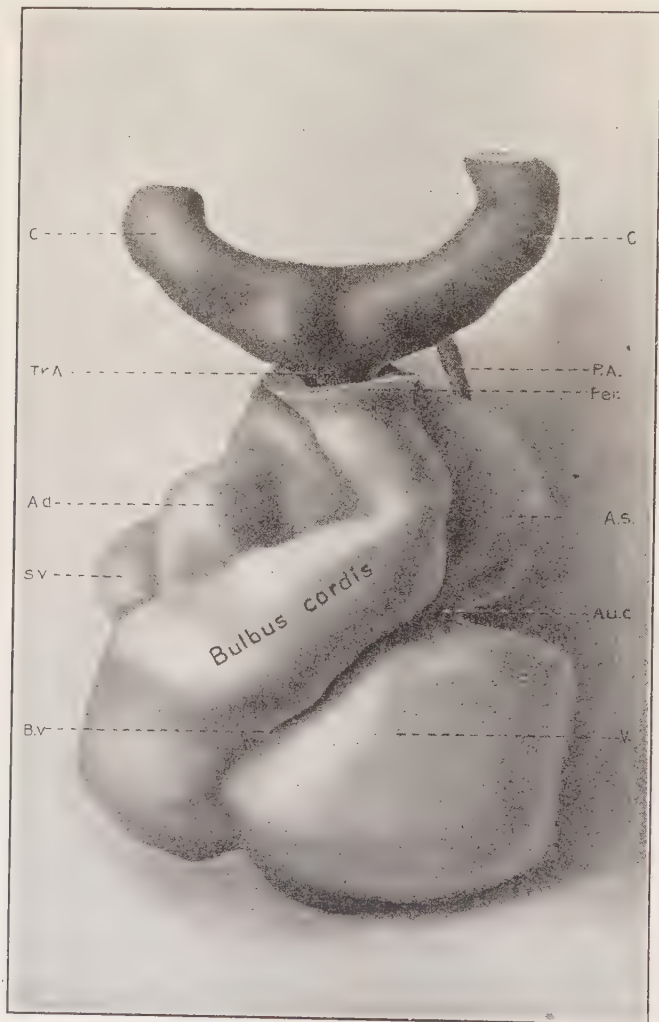
⁶ *Jour. Anat.*, London, 1917, 51, 19.

⁷ *Proc. Roy. Soc.*, Edinburgh, 1918-1919, 52, 257.

⁸ *Virchow's Arch. f. path. Anat.*, 1923, 243, 81.

the aortic arches. In the human embryo of 4 to 6 mm. in length the bulbus is a thick-walled muscular tube passing to the left and upward, lined like the rest of the heart with endothelium, which presents certain endo-

FIG. 39

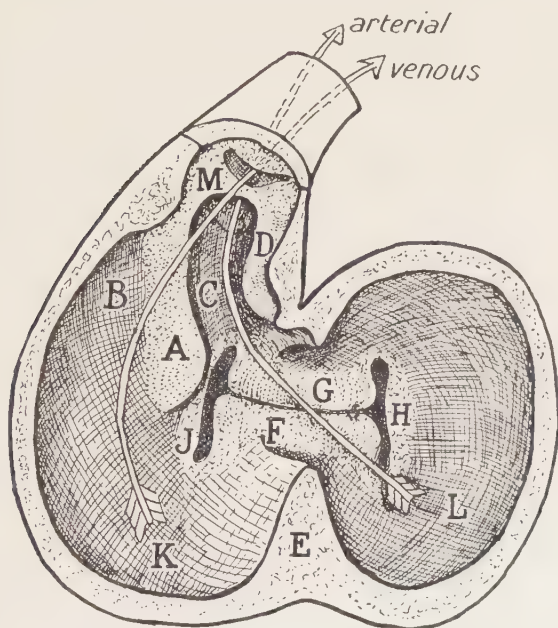


Model of the heart of a human embryo, 4.6 x 108 mm. (F. T. Lewis and M. E. Abbott.) (Dr. Begg's embryo.) *C*, Carotid arch; *P.A.*, pulmonary artery; *Per.*, pericardium; *Tr.A.*, truncus arteriosus; *A.d.*, right auricle; *A.s.*, left auricle; *S.v.*, sinus venosus; *A.u.c.*, common auriculoventricular orifice; *B.v.*, bulboventricular cleft; *V.*, common ventricle. (From the Anatomical Laboratory of the Harvard Medical School.)

cardial thickenings, *spirally arranged*, the so-called proximal and distal bulbar swellings, structures which later form the *anlagen* of the semi-lunar cusps as well as of the lower part of the aortic pulmonary septum. In later stages the bulbus disappears, its proximal portion undergoing

obliteration on the side of the left ventricle and becoming incorporated on the right side in the musculature of the expanded infundibulum and body (Waterston) of the right ventricle, and its distal part, denuded of its musculature and considerably elongated, constituting the primitive aortic trunk. The researches of Greil¹ on the reptilian, and Keith² on the human heart and of Jane Robertson³ on the fish, show that the

FIG. 40.



Diagrammatic presentation by J. E. Frazer of a reconstruction of the bulbar and infundibular region of a human embryonic heart in the sixth week, with anterior wall removed to expose the interior of the heart. The spirally arranged right and left bulbar endocardial swellings are seen approaching each other preparatory to fusing together to form the bulbar septum.

A, Right bulbar cushion dividing the infundibular or right part of the bulb (B) from the aortic or left part of the bulb (C); D, left bulbus cushion into which grows the musculature of the left septal band; E, interventricular septum; its musculature is entering the posterior endocardial cushion of the auricular canal (F); G, anterior endocardial cushion of auricular canal; H, left (mitral) orifice; J, right (tricuspid) orifice; K, right ventricle; L, left ventricle; M, interaortic septum with cushions of semilunar valves.

The arrows indicate the course of blood from the ventricles to the pulmonary and systemic divisions of the primitive aorta. (From J. E. Frazer: *The Formation of the Pars Membranacea Septi*, *Jour. Anat. and Physiol.*, 1917, 2, 19. Republished by Sir A. Keith, *Lancet*, 1924, ii, 1272).

mammalian bulbus represents what was at one time an independent chamber with muscular walls and its own system of multiple valves, which in the "ontogenetic telescoping of phylogenetic stages" has become submerged.

¹ *Morph. Jahrb.*, 1903, 31, 123.

² *Festschrift of the Quatercentenary of Aberdeen University*, July, 1906.

³ *Jour. Path. and Bacteriol.*, 1913, 18, 191.

Robertson correlates her findings in the fish with those of Greil in the lizard, and Born in the mammalian embryo, and traces the bulbus of the latter back through the less blurred stages of the reptile to the simpler forms seen in the Dipnoan and Elasmobranch fishes. Thus this structure, represented in the adult mammal, with its fully established double circulation, by the completely separated aortic and pulmonary trunks, is seen in *Lacerta* (reptile) to consist of a curved muscular tube divided by a spiral aorto-pulmonary septum, which gives way in turn in *Lepidosiren* (Dipnoan fish) to a kinked muscular tube with median expansion incompletely divided by rows of spirally arranged valves, and this again in the Elasmobranch fishes with their purely branchial respiration, is reduced to the simplest form as a straight channel with muscular walls lined by numerous rows of longitudinally placed valves. These phylogenetic proofs of an early bulbar channel with spiral division of its distal portion, are of the utmost importance in the elucidation of the problems of stenosis of the pulmonary conus and transposition of the arterial trunks, and yield striking confirmation of the explanations offered by Keith of the former, and Rokitsansky of the latter, anomaly. Sir Arthur Keith¹ outlines these advances, and stresses, in further elucidation of the complicated changes that take place in the critical bulbar region, the formative energy of developing endocardial tissue and the extraordinary power of invasion of this possessed by the primitive musculature, whereby the spirally arranged (and now fused) lateral bulbar endocardial cushions are replaced by the great muscular septal bands of the conus of the right ventricle (see Fig. 40), expansion taking place simultaneously of the infundibular part of its cavity, which is entirely bulbar in origin.

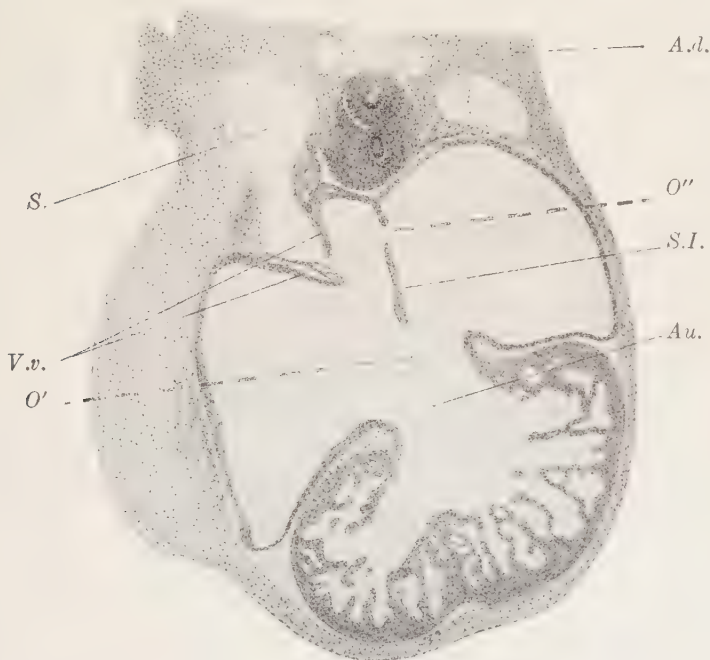
The Interauricular Septum.—According to Born, division of the auricles takes place through the development of *two different partitions* placed in planes parallel with each other developing successively, parts of which are temporary, while parts persist to form the permanent interauricular septum of postnatal life. The first of these, called by Born the *septum primum*, is the real division between the auricles. It begins about the fourth week from the upper and posterior wall of the auricle as a sickle-shaped fold which grows forward and downward toward the ventricular cavity and for some time an opening exists between the auricles at the lower border of this primitive septum known as the *ostium primum*. About the beginning of the fifth week a second opening, called by Born the *ostium secundum*, forms in the now greatly thinned upper and back part of the septum primum. This second opening grows larger as the ostium primum becomes smaller, and finally disappears entirely (end of fifth week), through the union of the expanded lower margin of the septum primum with the fused endocardial cushions between the auriculo-ventricular ostia. There thus exists a stage in development when the septum primum is represented by a band of tissue between two orifices, the ostium secundum above, and the ostium primum below. (See Figs. 41 and 42.)

The *septum secundum* is a name given by Born to a low ridge of tissue on the upper and posterior wall of the right part of the common auricle.

¹ *Lancet*, London. ii, 1924, 1267.

It was described by him as arising considerably later than the septum primum in a plane a little to its right, from the upper wall of the right auricle, and passing downward covering in the upper and anterior portion of the ostium secundum, thus giving it a valvular character and transforming it into the foramen ovale of fetal life. Recent embryological studies indicate that the secundum is not a true septum, like the septum primum, but is the result of pushing inward of the atrial wall from without by the conus arteriosus anteriorly (Retzer) and above and posteriorly by the coaptation of the infolded adjacent walls of the two atria at the point of junction of the valvula venosa sinistra with the septum primum (Waterston).

FIG. 41



Transverse section through the heart region of an embryo of 8 mm. greatest length. *A.d.*, descending aorta; *A.u.*, atrial canal; *S.*, sinus venosus; *V.v.*, valvula venose; *S.I.*, septum primum. Note the bifid apex seen at this stage and also the presence of two openings (*O'* and *O'''*) in the primitive auricular septum. In the collection of the I. Anatomical Institute, Vienna. (From Tandler's article in Keibel and Mall's *Embryology*, vol. 2, p. 549.)

The Interventricular Septum.—This begins about the fourth week, just after the origin of the auricular septum, as a crescentic ridge on the inferior wall of the ventricle. It grows upward and backward, its posterior limb merging with the corresponding walls of the ventricle and with the posterior endocardial cushion, and its anterior limb with the antero-ventricular wall, while its median curved portion unites along its right margin (Frazer) with a prolongation of the proximal aortic (bulbar) septum (the aortic orifice having moved over from the right to over-ride the ventricular septum), and with the fused endocardial cushions of the

auriculo-ventricular orifice (which has also come to lie in the median line), so that the ventricles are completely separated from each other and the arterial and venous ostia are placed one in either ventricle (Fig. 40). The point of union of the aortic with the interventricular septum, just below the adjacent ends of the anterior and left posterior aortic cusps, remains transparent and devoid of muscle throughout life, and is known as the *pars membranacea*, or undefended space.

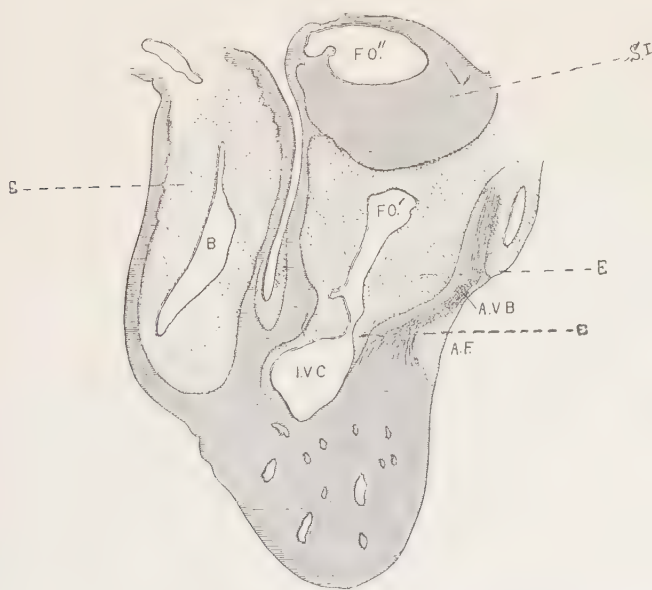
The Aortic Septum.—The *truncus arteriosus* is divided into the two great efferent vessels of the heart by a septum derived from three sources. Before the fifth week a sharp fold, the *aorto-pulmonary septum proper*, appears in the lumen of the truncus at the point of junction of the 4th and 6th arches (which represent respectively the aortic and pulmonary trunks) and grows rapidly downward. Some distance above the heart this aorto-pulmonary septum proper meets and fuses with a *spiral septum derived from fusion of the so-called distal and proximal endocardial bulbar swellings*. The bulbus cordis which forms, as stated above, by the involution of its proximal portion the termination of the ventricle, and by the elongation and demuscularization of its distal portion, the first part of the primitive aorta, is supplied internally with a series of endocardial elevations, of which four belong to its distal and two to its proximal part (known respectively as the Distal Bulbar Swellings 1, 2, 3, and 4, and Proximal Bulbar Swellings A and B of Born). These swellings, while symmetrically placed on opposite sides of the tube, have a spiral arrangement from above downward, and the distal swellings 2, and 4, which are much more prominent than the distal swellings 1 and 3, are directly continuous in clock-wise spiral fashion with the proximal swellings A and B. Fusion with each other, first of the more prominent pair of the distal bulbar swellings and later of the proximal ones occurs, the *spiral bulbar septum* resulting, which united at its distal end with the aortico-pulmonary septum proper, the two structures being clearly distinguished from each other by their distinctive histological characters.

The chambers of the heart and the two great arteries have thus been completely separated from each other before the eighth week of fetal life. Meantime, the right horn of the sinus venosus has been taken up in the wall of the right auricle, and the *valvula venosa sinistra* has disappeared, a portion of the *valvula venosa dextra* persisting as the *Eustachian valve*, and the left sinus horn remaining as the coronary sinus, while the left duct of Cuvier becomes obliterated (left superior vena cava). The pulmonary veins form later, opening at first as a single trunk, which is later taken up in the wall of the left auricle, thereby enlarging it. The semilunar cusps appear to form about the seventh week, from the proximal ends of the four distal bulbar swellings, two of which are subdivided in the descent of the septum trunci, so that six cusps, three placed in each artery, result.

The Auriculo-ventricular Cusps and the Atrio-ventricular Bundle of His.—The most critical point in the developing heart is undoubtedly the atrial canal. The endocardial cushions, which develop within it, are extensive and vitally important structures, not only as taking the essential part in the formation of the venous ostia, but also as completing the separation of all four chambers by fusion with their respective septa. Moreover,

from the observations of Mall on a large series of early human embryos, we learn that the differentiation of the auriculo-ventricular bundle of His is to be traced to the breaking of the continuity of the atrial with the ventricular musculature by the ingrowth of constricting epicardial connective tissue about the external surface of the atrial ring. Thus while in very early stages the muscle of the auricle is continuous with that of the ventricle at all points, in later stages a single band of atrial tissue passing down posteriorly from the lower border of the sinus venosus to the ventricle, and two minor fasciculi on the antero-lateral wall, are the only remaining connection between the chambers. The survival of these isolated portions in the general destruction of the muscular continuity between auricle and ventricle is explained by Mall by the anatomical relations of the posterior part of the interventricular septum, which, growing up toward the posterior endocardial cushion, pushes the epicardial tissue obliquely before it and permits the escape of a small portion of auricular muscle. This surviving atrial tissue, now the only path of conductivity, undergoes differentiation and later, innervation, and becomes readily identified as the auriculo-ventricular bundle.

FIG. 42



Sagittal section through the heart region of an embryo 8 mm. long, $\times 40$, No. 113 of Prof. Franklin P. Mall's collection. B, bulbus cordis; A.V.B., auriculo-ventricular bundle; A.F., annulus fibrosus; I.V.C., interventricular canal; F.O.', ostium primum; F.O'', ostium secundum; S.I., septum primum; E, endocardial cushions. Note the extensive development of the endocardial cushions within the auricle. (From the article by F. P. Mall in the *American Journal of Anatomy*, July 15, 1912.)

This contention of Mall, that the bundle represents persistent atrial tissue, and that its survival at this point is the result of its anatomical relation with the interventricular septum had already been suggested by Gaskell, and has received striking confirmation from the investigations

of Mönckeberg¹ and Sato² in the distribution of the bundle in various cardiac defects. Thus in a *cor triloculare biatriatum* where, in the entire absence of ventricular septum, one might conclude a destruction of auricular tissue in the whole circumference of the atrial ring, this bundle was found to be absent from the normal situation and was represented by a small band of tissue accompanying a small vessel on the antero-lateral aspect of the heart. In localized defects of the inter-ventricular septum at the base, in which the posterior part of the septum practically always remains entire, the bundle was seen intact in both ventricles, streaming over the lower border of the defect.

The auriculo-ventricular cusps are formed from the endocardial cushions of the atrial canal. These cushions are a series of elevations of the lining endothelium of the cardiac tube formed by a spongy connective tissue, and are four in number. Two, the anterior and the posterior, develop very early, become of large size, and, growing toward each other, fuse to form the wedge-shaped block which separates the venous ostia and completes the cardiac septa. In addition they encroach by their rapid growth on adjacent structures, so that they come to line the lower border of the *septum primum* in the auricle, while extending also by their apices into the depths of the ventricle. The lateral cushions, of smaller size, develop later, and, with the antero-posterior pair, are converted from endocardial structures into the musculotendinous valves, by the undermining of their substance from without, and by their own invasion of, and fusion with, the spongy musculature of the ventricle.

Primitive Aortic Arches.—It is now demonstrated that these number six instead of five, as Rathke described, the fifth arch being rudimentary in character. They are more or less evanescent in all animals, except fishes, in which five persist. In birds and mammals the first, third and fifth disappear on both sides. In man the fourth left arch becomes the aorta, the fourth right, the right subclavian, while the sixth pair become the pulmonary arteries.

LITERATURE

The rarity of cardiac defects, the obscurity of their etiology and symptoms, together with the fact that the cases are often of serious clinical import, make the subject of congenital cardiac disease of the highest interest. Since the time of Senac³ it has attracted the interest of many of the ablest workers in the field of cardiac pathology. There are important contributions from nearly all the earlier writers upon the heart, including Morgagni, Wm. Hunter,⁴ Meckel,⁵ Louis,⁶ Farre,⁷ Breschet, Sir James Paget,⁸ Gintrac,⁹ Chevers¹⁰ and Rokitsansky.¹¹ The first com-

¹ *Atlas der Herzmissbildungen*, Jena, G. Fischer, 1912.

² Aschoff: *Ber. d. Naturforsch. Gesellsch. zu Freiburg*, 1913, vol. 20.

³ *Traité de la structure du cœur, de son action et de ses maladies*, Paris, 1749.

⁴ *Medical Observations and Enquiries*, London, 1784, 6, 291.

⁵ *De Cordis conditionibus abnormibus*, Dissertation, Halle, 1802.

⁶ *Mémoires ou recherches anatomico-pathologiques*, Paris, 1826.

⁷ *On Malformations of the Human Heart*, London, 1814.

⁸ *Edinburgh Medical and Surgical Journal*, 1831, 36, 263.

⁹ *Récherches sur la maladie bleue*, Paris, 1824.

¹⁰ *London Med. Gaz.*, series of articles, 1845–1851.

¹¹ *Defekte der Scheidewände des Herzens*, Vienna, 1875.

prehensive study with a review of this earlier literature, may be said to be Peacock's¹ which remains a classic and is still a leading authority in English upon the subject. In Germany the ground has been covered by Lebert-Schrötter² (1879), by Rauchfuss³ (1878), by Vierordt⁴ (1898), in a statistical study of great value, by Thorel⁵ (1903 and 1911) and by Herxheimer⁶ (1910). In English there are the excellent general accounts of Humphry,⁷ Carpenter,⁸ Keith,⁹ Newton Pitt,¹⁰ John Thomson,¹¹ and M. E. Abbott,¹² and in French the work of Moussous,¹³ Girard,¹⁴ Thérémín¹⁵ and recently the brilliant clinico-pathological treatise by Laubry and Pezzi.¹⁶

Special Articles.—An important and brilliant original contribution to the *pathogenesis* of this subject was made by Rokitsky in his analysis of 44 cases of complicated septal defects, with combined study of the normal anatomy of the cardiac septa and of their development as observed by himself in the human and chick embryo. Rokitsky explained all cardiac anomalies as due to an arrest of development of the cardiac or aorta septa, producing irregular or non-union. While his conclusions have been modified by later observers, his work remains of great value as supplying a clue to many problems, especially that of transposition of the arterial trunks.

Reference has already been made to the fundamental work of Keith in the same field. From a series of personal observations on conus stenosis and the study of 270 malformed hearts in the London Museums, he advanced the view that cardiac defects are nearly always developmental in origin, that pulmonary stenosis is usually due to a persistence of the embryonic bulbus cordis, and that transposition of the great trunks usually results from an irregularity of involution of the same primitive structure. An interesting theory of the action of pathological currents in the blood stream as the cause of such an arrest of development has been advanced by Beneke.¹⁷ Mautner,¹⁸ quoting Spitzer, has presented the suggestive idea that persistence of the reptilian right aorta and submergency of the left, may take part in the pathogenesis of pulmonary stenosis with associated septal defect and certain forms of transposition in which the great trunks rise in reversed relations from the right ventricle; and the fact is adduced in support of this theory that in such cases of

¹ *Malformations of the Human Heart*, 1858 and 1866.

² Article in Ziemssen's *Handb. d. spec. Path. et Therap.*, Leipsic, 1879, vol. 6.

³ In Gerhardt's *Handb. d. Kinderkrankh.*, 1878, Part I, vol. 4.

⁴ Nothnagel's *Spec. Pathologie und Therapie*, 1898, vol. 15, Pt. I, Chap. 11.

⁵ Lubarsch and Ostertag's *Ergebnisse*, 1903, Chap. 1, p. 585; 1910, Chap. 11, p. 268.

⁶ Schwalbe's *Missbildungen*, 1910, Part III, Chap. 2, Lief. 3.

⁷ Allbutt's *System of Medicine*, 1898, 6, 697; 1909, 2d ed., 6, 276, 310.

⁸ *Brit. Jour. Child. Dis.*, 1909, 6, 337, 385, 433.

⁹ *Lancet*, 1909, ii, 359, 435, 519; 1924, i, 1267.

¹⁰ *Right-sided Valvular Lesions*, in Allbutt's *System of Medicine*, 2d ed., 1909, 6, 310.

¹¹ *Oxford Med.*, 1920, 2, 371.

¹² Osler and McCrae's *Modern Medicine*, 1908, 4, 323; 2d ed., 1915, 4, 323.

¹³ *Encyclop. Scient. des aide-memoires*, Paris.

¹⁴ *Rev. d. méd.*, 1900, pp. 645 and 837; *Jour. d. l'anat.*, 1909, pp. 1 and 323.

¹⁵ *Etudes sur les affections congénitales du cœur*, Paris, 1895.

¹⁶ *Traité des maladies congénitales du cœur*, Paris, J. B. Bailliere et Fils, 1921.

¹⁷ *Beitr. z. path. Anat.*, 1920, 67, 1.

¹⁸ *Jahrb. f. Kinderheilk.*, 1921, 96, 123.

developmental pulmonary stenosis the pulmonary valve is usually bicuspid (as in the reptilian heart), and a persistent right aortic arch is not an uncommon associated anomaly.

The hitherto obscure question of the causation of the symptom-complex of congenital cyanosis has been elucidated, in a remarkable degree, by Lundsgaard and Van Slyke¹ in their brilliant monograph on the "influencing" and "modifying" factors of cyanosis in general.

The problems of the pathogenesis of the other special symptoms of this complex, namely, polycythemia, clubbing and dyspnoea, are also brought close to final solution by the fundamental work of Krogh² on the capillaries and the discovery of capillary microscopy by Weiss and Lombard; by Parkes Weber's³ revision (1922) of his earlier contributions on the subject of secondary or symptomatic polycythemia as a compensatory vital process; and by many other contributions.

On the *clinical* side great advances have been made in recent years in our understanding of the nature of congenital cyanosis, and in the differentiation of various types of disease, based on the pathological physiology of the altered circulation in the different defects. The first clear delineation of the contrasting features of the so-called "cyanotic" and "non-cyanotic" groups of congenital cardiacs was made by the French writers. Thus Fallot⁴ pointed out that the "tetralogy" of pulmonary stenosis, interventricular septal defect and dextroposition of the aorta with hypertrophy of the right ventricle, is by far the commonest underlying condition in patients with congenital cyanosis reaching adult life, and that in cardiac septal defects *without* associated pulmonary stenosis cyanosis is usually absent; Roger⁵ (1879) established *absence of cyanosis in the presence of distinctive physical signs* as the characteristic clinical picture in defect of the interventricular septum (*maladie de Roger*), while Bard and Curtillet⁶ (1889) extended this observation to defects of the interauricular septum and showed that the advent of a "late" cyanosis, appearing during the last weeks or months of life in a person who had previously shown no signs of oxygen unsaturation, was the usual termination in patent foramen ovale, and this course of events has been shown by later observers to be characteristic of all forms of cardiac septal defects. The absence or presence of an abnormal communication between the pulmonary and systemic circulations, and the direction through this of the "shunt" of the anomalous current of blood, whether arterial-venous or venous-arterial, has been made the basis of a clinical classification formulated by M. E. Abbott⁷ and illustrated by diagrams constructed by W. T. Dawson, which successfully present in graphic form the course of the circulation in the various defects. The suggestive term, "intracardiac fistulae," has been proposed by Emil Holman⁸ for such septal communications and an attempt has been made by this writer to supply the information gained by experiment in acquired

¹ *Medicine*, 1923, 2, 181.

² *The Anatomy and Physiology of Capillaries*, Yale University Press, 1922.

³ *Polycythemia, Erythrocytosis and Erythræmia*, P. B. Hoeber, 1922, p. 148.

⁴ *Marseille méd.*, 1888, 25, 77, 138, 202, 270, 341, 403.

⁵ *Bull. de l'acad. de méd.*, 1879, 8, 1074.

⁷ *Internat. Clin.*, 1926, 2, 155.

⁶ *Rev. de méd.*, 1889, p. 993.

⁸ *Arch. Int. Med.*, 1925, 36, 516.

arteriovenous aneurism (Lewis and Drury, *et al.*) to communications between the two circulations through a patent ductus or defective septum; the new factor introduced here by the muscular action of the right heart, renders conclusions drawn from any such parallel extremely problematical, but the comparison opens up a field of extraordinary interest. In this connection the important embryological and clinico-pathological study on congenital arteriovenous aneurism by Rienhoff¹ (with full bibliography) is a valuable and welcome addition.

Other important advances along clinico-pathological lines are the topographical and histological studies by Mönckeberg, Keith, Morison and others into the course of the auriculo-ventricular functional fibres in various defective conditions of the cardiac septa, and especially the recent valuable communication by Wilson and Grant on the anomalous distribution of the bundle in a case of congenital partial heart block in complete absence of the interventricular septum.

Modern advances in *laboratory procedures*, and such *aids to diagnosis* as are supplied by the polygraph, electrocardiograph, roentgen-rays, gas-analytic methods, etc., have contributed substantially to the differentiation and clearer definition of the various clinical types of congenital cardiac disease. Characteristic findings are recorded by Vaquez and Bordet,² Assmann,³ Dietlen,⁴ Lewis,⁵ Parkes Weber,⁶ Plesch,⁷ Meakins⁸ and many others. The first complete study of the blood volume, blood-gas findings and oxygen capacity in a case of congenital cyanosis, of which we know was published by Parkes Weber and Dörner⁹ in 1911. A valuable and very comprehensive investigation has also appeared in the joint article by Raab, Weiss and Lowbeer and Rühl¹⁰ (1924) in a case of pulmonary stenosis with septal defect (Fallot's tetralogy) confirmed by autopsy, in which the roentgen-ray picture, graphic tracings, respiratory metabolism and blood-gas changes, with computation from the data so obtained of the amount of the venous-arterial shunt through the defect, are given in full detail.

A very important contribution from the *clinico-pathological* side is the recent classic study by Thomas Lewis and R. T. Grant,¹¹ on the architecture of congenitally bicuspid aortic valves, and the invasion of these by an acute endocarditis, with results obtained which amplify and confirm the earlier observations of Sir William Osler¹² on the subject. The frequent *incidence of bacterial endocarditis in cardiac defects* has been emphasized also in articles by James Paget, A. Garrod,¹³ Parkes Weber, Thos. Horder and, more recently, by Blumer, Libman, and Abbott¹⁴ (full bibliography).

¹ *Johns Hopkins Hosp. Bull.*, 1924, **35**, 24.

² *Le cœur et l'aorte, études de radiologie clinique*, Paris, 1924.

³ *Klinische Röntgendiagnostik*, Vogel, Leipzig, 1912.

⁴ *Herz und Gefässe in Röntgenbild*, Leipzig, J. A. Barthy, 1923.

⁵ *Clinical Electrocardiography*, 1924, p. 112.

⁶ *Practitioner*, London, April, 1908.

⁷ *Berl. klin. Wchnschr.*, 1909, **46**, 390.

⁸ *Heart*, 1923, **10**, 153.

⁹ *Lancet*, 1911, i, 150.

¹⁰ *Wien. Arch. f. klin. Med.*, 1924, **7**, 367.

¹¹ *Heart*, 1923, **10**, 21.

¹² *Trans. Assn. Am. Phys.*, 1886, p. 185; *Quart. Jour. Med.*, 1909, **2**, 219.

¹³ *St. Bartholomew Hosp. Repts.*, 1899, **35**, 148.

¹⁴ *Ann. Clin. Med.*, 1925, **4**, 189.

From the standpoint of *treatment* operative interference recommended by Carrel in pulmonary stenosis, and carried out with success by Cutler and Levine¹ in mitral stenosis, is an advance that brings a ray of hope to at least some of the unfortunate cases of "*morbus cœruleus*," although it is scarcely past the experimental stage. The necessity of early recognition of cardiac septal defects of the "non-cyanotic" type and of according to these the same preventive care in the avoidance of focal infections and cardiac strain as is accorded to the "potential cardiac" is insisted upon by Abbott.²

The present article is based upon the statistical study of 850 defects with autopsy findings; of these, 205 have been drawn from the *Transactions of the Pathological Society of London* and the balance from the literature elsewhere and from personal experience. The results obtained are considered below under the subjects named and in the order given in the statistical chart attached.

ETIOLOGY OF CONGENITAL CARDIAC DISEASE

Cardiac anomalies may be divided, according to etiology, into two main groups: those due to *arrest of growth* at an early stage, before the different parts of the heart have been entirely formed, and those produced in the more fully developed heart by *fetal disease*.

Arrest of Growth.—From the earliest times search has been made for the underlying causes of the arrest of development manifest in cardiac malformations. Long before Darwin, Meckel, in 1812, pointed out the resemblance of certain defects to the hearts of those animals, which present in a stationary form the different stages through which the mammalian heart passes in its development, and explained them as reversions to a more primitive type.

In seeking the causes of the defect we may turn first to the study of associated anomalies. Do these occur in such frequency and constancy as to place their combination beyond the range of coincidence? And if so, may the causes leading to malformations elsewhere, such as disease and adhesions of the amnion or disease of the mother or germ plasm, or hereditary predisposition, be assumed to act upon the fetal heart?

In Rokitansky's *Defekte der Scheidewände des Herzens*, among 24 complicated defects of the septum, all evidently of developmental origin, associated anomalies such as transposition of the viscera, cleft palate, etc., occurred in 8, that is, in one-third of the cases. Vierordt, in the 700 cases reviewed by him, found associated anomalies in 80 (11 per cent.). On the other hand Keith found among 23 malformed fetuses and infants showing anencephaly, hydrocephaly, spina bifida, umbilical hernia, atresia ani, cleft palate, harelip, and stricture of the œsophagus, in 14 a malformation of the heart.

Among the 850 cases studied here, anomalies elsewhere in the body, among which may be enumerated malformations of liver and lung,

¹ *Boston Med. and Surg. Jour.*, 1923, **188**, 1923; *Arch. Surg.*, 1924, **9**, 689.

² Blumer-Billings: *Forscheimer's System of Therapeutics*, New York, Appleton & Co., 1924, **4**, 322.

asymmetry of calvarium, partial or complete transposition of viscera, harelip and cleft palate, encephalocele, gastro- and rachischisis, absence of spleen or kidney, diverticula, hypospadias, hernia, etc., occurred in 144 cases, that is, in 17 per cent. Defect of the interventricular septum was associated in Chaffey's case with imperforate anus, in Moore's with a supernumerary thumb, in Morestin's with syndactylism and absence of femur, fibula, and genitalia. A widely patent foramen ovale was combined in Berthel's case with rudimentary genitalia, and in Tylecote's with a congenital perforation of the nasal septum. Kingsley reports patent ductus with macroglossia and absence of the left kidney, and Dick a case of pulmonary artery forming the descending aorta, with the uterus bipartite and the kidneys fused, and Watton and Abbott¹ a case of parasitic thoracopagus with transposition of the arterial trunks and cor biloculare biatriatum in the autosite, which attained the age of fourteen months and presented a moderate cyanosis. In the valuable developmental study by H. A. Harris² of a fetus miscarried in the twenty-seventh week with cor biventriculare triloculare with bifid apex, persistent left superior cava and persistent right aortic arch with absence of the transverse arch and left arch giving off the left subclavian and forming the descending aorta through the patent ductus, there were present in addition marked skeletal deformities (absence of left half of body of eighth and ninth dorsal vertebrae and eighth and ninth ribs and scoliosis, absence of the left lung, left pleural cavity, kidney, ureter and renal artery, atresia ani et recti, atresia of upper part of oesophagus and left broncho-oesophageal fistula. Mental deficiency or derangement of the higher nerve centres is not infrequent, although intelligence is sometimes above the average. Thus idiocy was reported by Simmons, Carpenter and Rheiner, in cases of patent foramen ovale, patent ductus and septal defect respectively, and in a biloculate heart reported by Dublitzhaza, idiocy was combined with strabismus and pes varus. The frequent association of cardiac anomalies with the Mongolian form of idiocy has been noted by A. E. Garrod³ and John Thomson. The latter relates that in 300 cases of this condition there were symptoms of congenital cardiac disease in every 6 cases below five years, and in 1 in 8 of the older children. In the writer's experience the commonest cardiac anomaly in Mongolian idiocy is a defect of the interauricular septum, especially persistent ostium primum,⁴ a fact which may throw some light on the stage of the developing embryo at which the causes producing the condition operate.

H. A. Harris⁵ has published the interesting combination of extensive defect of the aortic system (persistent truncus arteriosus with right aortic arch) with congenital cystic elephantiasis and phocomelus (dwarfing of the extremities), all of which defects fall within the critical period of time (sixth week), both for the cardio-respiratory, lymphatic, and skeletal systems, and are probably due to the action of a cause operating at that

¹ *Bull. Int. Ass. Med. Mus.*, 1923, **8**, 165.

² *Jour. Anat.*, 1922-1923, **57**, 76.

³ *Trans. Clin. Soc. London*, 1899, **32**, 6.

⁴ Abbott, M. E.: *Persistent Ostium Primum in Mongolian Idiocy*, *Bull. Int. Assn. Med. Mus.*, 1924, **10**, 111.

⁵ *Am. Jour. Obst. and Gynec.*, 1926, **40**, No. 6.

time. An associated defect of the heart is always present with congenital lymphangiectasis but the causal relationship of the two conditions is not understood.

Further illustrations might be multiplied, but the above suffice to show that the association of grave anomalies with cardiac defects is too frequent to be considered accidental. That the cause of both is to be sought, not so much in a hereditary predisposition, as in a diseased condition of the fetal envelopes or of the maternal tissues is evident from the facts yielded by the family history of these cases. For a history of congenital disease in the ancestry is much less common, than is one of cardiac defect or other anomaly in other members of the same generation, and evidence of infective processes or depressing influences acting within the parental organism is still more frequently supplied. In this series there was a history of congenital defect in a brother or sister of the patient in 11 cases, of rheumatism or heart-disease in the parents in 13, and of small-pox or tuberculosis in six. Congenital syphilis in the father was recorded by Jacobi, in a case of ectopia cordis, and lues whether congenital or acquired is certainly a frequent cause. Baneful influences may act upon the mother during the early weeks of pregnancy, such as great trouble, ill-treatment and fright. Severe inflammation of the bladder of the mother in the third month was blamed by Habershon for the development of pulmonary atresia with septal defect, and an operation on the mother for appendicitis was noted by Royer and Wilson in their case of incomplete heterotaxy.

Difficult delivery occurred in the cases of patent ductus by Luys, Roeder and others. In not a few instances the parents had both reached advanced middle life, and in some the child was the last of a series of many pregnancies. Laine reported a case of aortic stenosis with septal defect from a mother, aged forty-eight years, who had had four other children, of whom three were feeble-minded. Of much interest also is a specimen reported by J. McCrae, in which transposition of the viscera and atresia of the pulmonary artery were found in the fifteenth child of a mother, aged forty-six years, who was herself of poor intelligence and had a harelip.

The parallel seen in Mongolian idiocy, which also usually occurs in elderly parents and in the last of many pregnancies as what appears to be an "exhaustion product," is extremely suggestive. The fact, however, advanced by Halbertsma¹ and others, that Mongolian idiocy in twins never affects both members when these are of different sexes, *i. e.*, are indisputably the result of a multiovular twin pregnancy (thus pointing to a disorder of the germ plasma as a cause), must, however, be harmonized with any theory of a common origin of the cardiac anomaly.

The predominating cause of the defect is thus clearly to be sought, in the majority of cases, in the environment of the developing embryo. The early death in most cases of congenital cardiac disease, however, prevents direct transmission of cardiac defects, which might otherwise occur, and this lessens the apparent frequency of heredity. That

¹ *Am. Jour. Dis. Child.*, 1923, 25, 350.

heredity is a factor in a certain small proportion of cases is evidenced by various facts. Thus the association of polydactylism is significant when one considers the well-known familial tendency of this anomaly.

Fetal Disease.—*Fetal endocarditis*, which was believed by the earlier writers to play such an important part in the causation of cardiac anomalies, probably occupies a very minor role, being limited to those relatively few cases in which a rheumatic endocarditis is directly transmitted from the mother to her offspring. Of far greater importance are undoubtedly the *myocardial changes* which occur as a result of congenital syphilis or other infection carried in the coronary stream. Careful investigation of the myocardium in most cases of atresia of the orifices will reveal patchy

FIG. 43



Perivascular cell infiltration, extensive fibrosis and myocardial degeneration of the right ventricle in a case of transposition of the arterial trunks and atresia of the (transposed) aortic orifice from an infant, aged seven days.

yellowish-gray areas visible to the naked eye, which microscopically show all stages of degeneration, vacuolation, fatty change and even, in a case under the writer's personal observation, calcification with cellular infiltration, and a diffuse fibrosis, which is often myxomatous in character, recalling Warthin's¹ description of "focal fatty degeneration associated with localized colonies of *Spirochæta pallida*." The lesions tend to lie directly beneath the endocardium which in certain areas may present a proliferated and myxomatous structure resembling the embryonic endocardial cushions. The microscopic appearances in a case in which the

¹ *Jour. Am. Med. Assn.*, 1912, 58, 409.

arterial branches were transposed and the aortic orifice was atresic are figured here (Fig. 43). The semilunar valves were here intact and the fusion lay in the musculature of the conus directly below these. The possibility is suggested that the pathological changes in the myocardium have inhibited involution of the bulbar endocardial swellings and the invasion of these by the primitive musculature of the ventricle, and that fusion has occurred in their irregular involution. In a case of aortic atresia reported by Suvalischin (quoted by Loeser¹) the aortic cusps were rudimentary swellings of cellular tissue without trace of inflammatory action.

Reference to these myocardial changes is absent from the literature except in a few articles, of which the most important are those by Le Tulle,² von Zalka³ and Stiassing. Von Zalka studied the myocardium in 14 cardiac anomalies, 8 of which were due to true arrest of development (septal defects) and 6 were stenoses or atresias of the pulmonary or aortic orifices. In every one of the latter he found the myocardial changes above described. He concludes that in cardiac anomalies not due to a primary arrest of development myocardial disease is the usual cause. This applies to the valvular stenoses and atresias and probably also to certain conditions of cases of arrest in which fetal disease has set in at a very early stage of embryonic life.

CYANOSIS

Congenital cyanosis is a bluish discoloration of the skin and mucous membranes, characterizing those cases of congenital cardiac disease in which there is serious interference with the circulation leading to a pathological increase in the amount of reduced hemoglobin in the circulating blood. It differs from the cyanosis of the later stages of acquired cardiac lesions in that it may exist for many years without any signs of cardiac insufficiency. Its constant association with the other evidences of oxygen-unsaturation—dyspnoea and clubbing—raises it almost to the rank of a disease entity, and such, under the titles *Cyanopathia* or *Morbus Cæruleus*, it was long believed to be.

Pathogenesis.—The immediate causation of cyanosis has been the subject of much debate and of a great deal of confusion of thought, which is gradually becoming resolved as our knowledge of the physiology of the circulation advances. By the older writers it was variously ascribed to (a) venous stasis, (b) admixture of venous with arterial blood, (c) deficient aëration, (d) dilatation and new formation of capillaries in the lungs or (e) the peripheral parts of the body, (f) changes in the blood itself, *i. e.*, polycythemia. In the light of our present knowledge, each one of these conditions may in a given case produce or assist in producing the pathological increase of oxygen-unsaturation, and, according to their capacity in this regard, may be recognized as (a) essential or influencing factors in the production of the cyanosis that is the expression of such

¹ *Arch. f. klin. Med.*, 1915, **219**, 309.

² *Presse méd.*, 1914, **22**, 436.

³ *Frankfurter Ztschr. f. Path.*, 1924, **30**, 144.

de-oxygenation; or (b) factors that may take part in "heightening" or "modifying" the effects of such a raised unsaturation in the capillary circulation and so altering the "threshold value" at which the resultant cyanosis will appear (Lundsgaard). In the minds of the older observers, however, with all their astute clinical sense and keen observation of the pathological conditions presented, such an interdependence of these as primary and subsidiary causes, was scarcely suspected, while the question of the proportion to which the reduced hemoglobin in the blood must rise before it becomes manifest by the cyanotic hue, was not even formulated. In the words of Lundsgaard and van Slyke, "Each of these theories contained a part but none the whole of the truth." Before further outlining the present status of our knowledge on this subject it will be instructive to trace the growth of these apparently conflicting ideas into actual harmony.

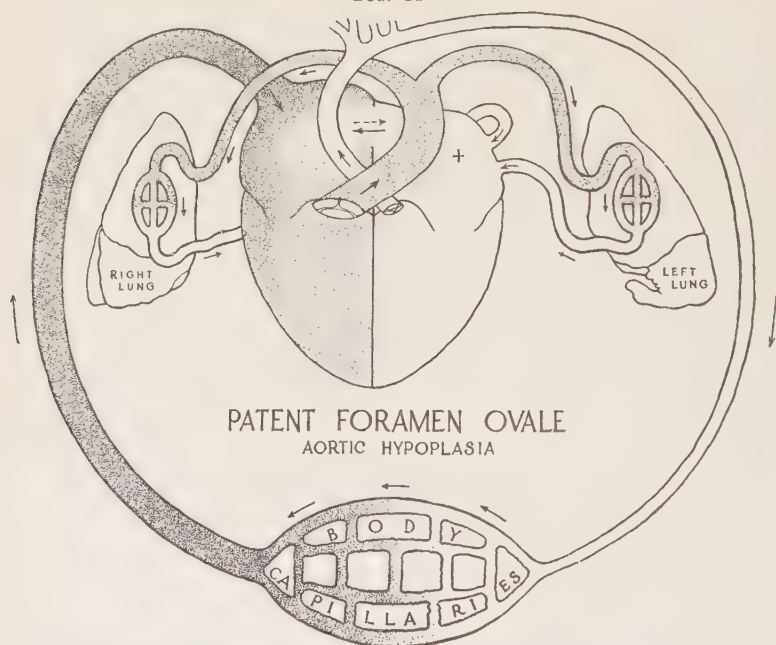
(a) The term *venous stasis* was used in this connection to imply obstruction to the free entrance of blood to the lungs and the resultant back-pressure in the systemic circulation. This theory, first advanced by Morgagni (1761), and supported by Louis and Peacock, was widely accepted but did not appear to explain the situation completely. It was difficult to understand how a simple venous stasis from obstruction at the pulmonary orifice could be sufficient to lead to cyanosis, through lagging of the blood in the systemic capillaries, and yet remain unassociated with the œdema and anasarca accompanying back pressure from other causes; and, on the other hand, the late appearance of the cyanosis in many cases of pulmonary stenosis, in which the defect had undoubtedly been present at birth, rendered it evident that some other factor, in addition to the mechanical difficulties which the lesion itself presented was needed to bring it about. A highly instructive case was published by Lafitte¹ of a young woman, dying at the age of twenty-one years of a malignant endocarditis, who had always been dyspnoëic on slight exertion but had never presented any sign of cyanosis. At autopsy the right heart was hypertrophied and about 1 inch below the pulmonary valves there was a fibrous annular stenosis of the infundibular orifice which was further blocked by large recent vegetations. Peacock, in reporting a similar case of pulmonary stenosis without cyanosis, suggested that the absence of symptoms was due to the marked hypertrophy of the right ventricle which had succeeded in sending sufficient blood to the lungs for aëration.

(b) The theory that cyanosis is due to a *mingling of venous with arterial blood*, advanced by de Senac (1749), and supported by Gintrac and Corvisart, but was apparently successfully refuted by many authorities, notably Peacock, on the ground that cyanosis is frequently conspicuous by its absence in cases in which a free admixture of venous with arterial blood has undoubtedly occurred. The classical illustration was Breschet's case, in which the left subclavian arose from the pulmonary artery, and yet the left arm was not discolored. Again, in some instances of biloculate or triloculate heart there is a complete absence of cyanosis at least until

¹ *Bull. de la Soc.*, 1892, 6, 13.

near the close of life. Thus Young¹ reported a cor biatriatum triloculare, both auricles opening into a common ventricle, from which arose the aorta and pulmonary artery, transposed and separated from each other by an anomalous septum, in a man, aged thirty-six years, who showed no cyanosis until the last three years of life. Peacock quotes an almost identical case in an infant aged eight months, with only a slight blueness of the lips during dyspnoeic attacks. Equally striking was a case of persistent truncus arteriosus, in which, although the blood from both ventricles entered the common arterial trunk, cyanosis was absent.

FIG. 44



(a) Arterial-venous shunt with terminal reversal of flow in patent foramen ovale. The black arrow shows the direction of the anomalous current from left to right through the defect under physiological conditions. The dotted arrow shows the current in the right to left shunt of the current in a terminal reversal of flow (*cyanose tardive*). Diagram by W. T. Dawson. From the *Clinical Classification of Cardiac Defects*, by M. E. Abbott and W. T. Dawson, *Internat. Clin.*, 1924, 4, 164, Fig. 6.

This theory of admixture of currents was however revived by Bard and Curtille² in a form that won general acceptance, even before the fact was grasped that oxygen-unsaturation must reach a certain level before cyanosis becomes manifest. They describe as *cyanose tardive* a cyanosis occurring as a terminal event, often at the end of a long life, in cases of patent foramen ovale, when some embarrassment in the pulmonary circulation causes a raised pressure in the right heart leading to a reversal flow of blood from right to left through the foramen and some-

¹ *Med. Chron.*, Manchester, 1907-1908, 14, 96.

² *Rev. de Med.*, December, 1889.

times to a forced reopening when it has been closed. They quote an illustration in a man aged fifty-four years, with patent foramen, dying of bronchopneumonia. Long before this, Peacock¹ reported such a case, in a woman, aged twenty-four years, with marked spinal curvature and widely patent foramen ovale, in whom marked cyanosis set in for the first time in the last months of life. Since then many such cases have been reported, and it is now well recognized that "late" or "transient" cyanosis from alterations in pressure producing a terminal or transient reversal of flow through the defect, is characteristic of all uncomplicated cardiac septal defect and of most cases of patent ductus arteriosus. Both Corvisart and Bamberger had pointed out this possibility but it was this careful clinico-pathological study of Bard and Curtillet that first established Senac's "admixture" theory as correct, at least for the cyanosis appearing in this group of cases. Later observations have demonstrated, upon experimental evidence, that the same reasoning applies in those graver cardiac anomalies (pulmonary stenosis with associated septal defect, biloculate or triloculate heart, transposition of the great trunks, etc.) in which cyanosis is a persistent and permanent feature. Thus Haldane and Douglas noted that the blueness in a case of congenital cyanosis did not yield to the administration of oxygen; so concluded it could not be due to lowered pulmonary ventilation; and Campbell, Hunt and Poulton² argued that the low values of oxygen saturation in the arterial blood obtained in 5 cases of congenital cyanosis investigated by them, could only be produced by the direct entrance into this of venous blood, since retardation of flow in the lungs should not in itself lead to deficient oxygenation of the blood there, but rather to its increased aëration. This deflection, by the mechanical conditions imposed by the defect, of an anomalous venous current into the arterial stream, is the chief cause, the "influencing" or essential factor in the great majority of cases of morbus cœruleus.

A few rare cases in the literature of pulmonary stenosis with *closed septa* (reported by Peacock, Reid, Ogle, Ormerod, Hebb), in which no path of exit for a venous-arterial shunt existed, supply further evidence against the old theory of "venous stasis," for in these subjects, all of whom attained adult life, cyanosis was absent or "slight" and could therefore probably be explained by the stasis in the capillaries which the pulmonary stenosis would tend to induce.

The fact that the most marked cyanosis with clubbing may occur in pulmonary emphysema and bronchiectasis, where no septal communication exists, supplied an argument formerly much adduced against the "admixture" theory. But here lies one of its best illustrations. In bronchiectasis, as Thomas³ points out, areas of loss of substance occur, and tortuous dilated capillaries with thickened walls exist, and it is readily conceived that in certain areas blood may pass from pulmonary arterioles to venules without undergoing due oxygenation by the way. In congenital cardiac disease dilatation and thickening of peripheral

¹ *Trans. Path. Soc.*, London, 1859, 10, 108.

² *Jour. Path. and Bact.*, 1923, 26, 234.

³ *Zeit. f. klin. Med.*, 1901, 41, 58.

vessels form a part of the picture, and alterations in the lungs very similar to those in bronchiectasis occur. In a case described by Carpenter¹ the lungs were loaded with pigment, their capillaries dilated to three times their normal size, crowded with red cells, elongated, tortuous, their walls thickened and rich in young fibrous tissue elements. Must not many red cells have passed through these thickened channels without receiving their due share of oxygen, and the blood have been thus returned, still largely venous in character, to the left heart?

(c) The theory that a variety of causes, including some or all of the possibilities above enumerated, lead to a deficient *aëration of the blood and that this is the essential element in the production of cyanosis*, has been formulated by all recent observers. There is abundant evidence to show that, whatever the path by which oxygenation is reduced, whether by direct influx of venous blood into the arterial tree, or by obstruction to the entrance of venous blood into the pulmonary circulation, deficient oxygenation is in all cases of congenital cyanosis the immediate cause of the symptomatology. The characteristic picture can be traced through the development of the compensatory mechanism of right heart hypertrophy, increased respiratory activity, and polycythemia, to the point where all these processes fail to supplement the inefficient pulmonary circulation with oxygen sufficient for the body needs. The chronic asphyxia that develops is expressed, not only in the cyanotic hue of the patient, but also in the alterations at the periphery of clubbing and retinal changes. These are the direct results of delayed and toxic tissue metabolism,² and an overloaded systemic circulation.

These considerations may be summarized by saying that the dependence of congenital cyanosis upon deficient oxygenation is now definitely established; that the circulation evidently accommodates itself to a certain degree of oxygen-unsaturation, whether brought about by obstruction in the course of the pulmonary artery, by a general retardation of flow, or by a mingling of venous with arterial blood, but that as soon as deficient oxygenation reaches a certain limit, this becomes insufficient for the needs of the body, and cyanosis results. That dilated peripheral capillaries, dark color of the skin and increased red cell content of the blood, must, when present, add their part to heighten the degree of discoloration is self-evident; but being themselves secondary, these conditions are not to be looked upon as etiological factors, but rather as concomitant effects of a common cause. Lastly, in complicated cardiac defects probably all the factors enumerated combine to produce the mulberry hue and the respiratory distress of the typical *morbus cœruleus*.

Analysis and Quantitative Determination of Causative Factors.—The advances within the last three decades in our knowledge of the respiratory function of the blood and the physiology of the circulation, of the rate of flow and minute volume of the blood as calculated from its gaseous contents and dissociation curves, the studies on vital capacity and hydrogen-ion concentration, and the accumulated results of investigations into tissue metabolism, have all paved the way for quantitative researches

¹ *St. Thomas Hospital Reports*, 1890, **18**, 285.

² *Deut. Arch. f. klin. Med.*, 1910, **99**, 382.

such as may convey a more exact understanding of the principles underlying the phenomena of cyanosis. The monograph by Lundsgaard and Van Slyke¹ is of extraordinary value for the elucidation of the symptomatology of congenital cardiac disease. On this account a brief exposition of its substance is necessary here.

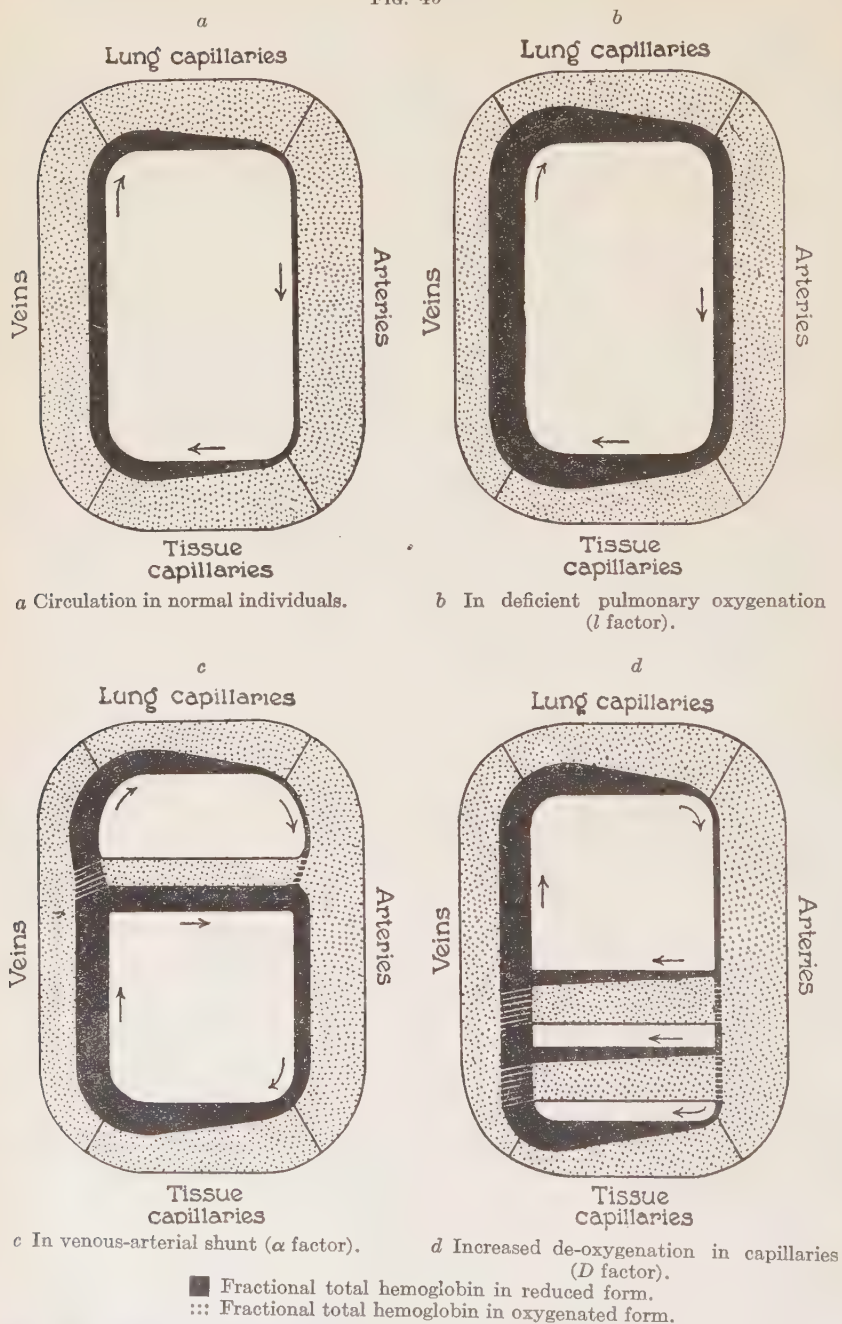
Starting from the principle, experimentally determined, that the cyanosis under consideration is produced by an increase of the reduced hemoglobin in the capillary circulation above a definite "threshold value" (6.7 per cent), they begin by classifying the heterogeneous series of possible causes of such an increase, into (a) "*modifying factors*" which may alter the "threshold value" of oxygen unsaturation at which the visible manifestation of cyanosis may appear, but which cannot in themselves produce such an increase; these are thickness or pigmentation of the skin, altered color of the plasma, raised hemoglobin content of the blood, and (most important of all) the variations in the number, width and extent of skin capillaries; and (b) "*influencing*" (or determining) *factors*, which directly produce cyanosis by raising the oxygen-unsaturation of the capillary blood above its "threshold value." These causative factors may act in two ways, either by lessening oxygenation in the lungs or by increasing oxygen consumption in the tissues, and they are four in number, as follows: (1) *Lessened or retarded oxygenation in the alveoli of the lungs* through lowered oxygen tension, insufficient pulmonary ventilation, etc. To this factor the symbol *l* is given (see Fig. 45), and since the oxygen capacity of the blood is 20 volumes per cent, and the blood leaves the lungs 95 per cent saturated, it follows that a single volume of oxygen-unsaturated blood leaves the lungs under physiological conditions, so that the value of *l* is 0.05 per cent. This factor *l* is the cause of cyanosis of high altitudes, of influenzal pneumonia, etc., both of which respond quickly to the administration of oxygen by the respiratory tract. It takes, however, relatively little part in the cyanosis of congenital origin so that the effect of linbreathing of oxygen is of diagnostic value in this regard. Campbell, Hunt and Poulton found that a pulmonary factor apparently took part in the production of oxygen-unsaturation in a case of congenital cyanosis investigated by them, since a definite percentage of the oxygen-unsaturation (but not the whole pathological increase) cleared up on administration of oxygen. This observation is one of great significance. The patient was a male aged twenty years, with red cell count of 9,300,000, and an arterial oxygen-saturation of 68.7; administration of oxygen by the lungs raised this to 91.1 per cent, instead of to 100 per cent as would have been the case had the low oxygen-saturation been only of pulmonary origin. These authors² noted also a lowered oxygen percentage saturation in a case of true erythremia with normal heart and lungs and ascribed it in both cases to the polycythemia in that the dilated pulmonary capillaries become overcrowded with red cells so that a proportion of these escape into the pulmonary veins without aëration.

2. The second influencing factor is from the outset a pathological condition, being the "right to left" shunt of an anomalous stream of venous

¹ *Medicine*, 1923, 2, 1.

² *Jour. Path. and Bact.*, 1923, 26, 234.

FIG. 45



Diagrams by Lundsgaard and Van Slyke, showing proportion of oxy-hemoglobin to reduced hemoglobin in: *a*, different parts of the circulation in normal resting individuals; *b*, in different parts of the circulatory system in a case of incomplete oxygenation in aerated parts of the lung (*l* factor); *c*, in a case where a fraction of blood passes through unaerated channels from venous to arterial system (α shunt); *d*, where de-oxygenation is abnormally high in a part of the peripheral capillaries (*D* factor). Reprinted from *Medicine*, 1923, 2, 16 and 19. By permission of Messrs. Williams and Wilkins.

blood into the arterial stream such as takes place through a *cardio-vascular* septal defect or in the obliterated areas of lung tissue as in emphysema. This has been already stressed as being the chief causative agent in congenital cyanosis. It is named by these authors α (*alpha*) and has a normal value of 0 as it does not occur in a physiological state of the circulation (Fig. 45c).

3. The third influencing factor (termed *D*), is an *increased reduction of oxygen in the tissue capillaries*, produced either by a retarded rate of flow in these or by an increased oxygen consumption in the tissues. Since the arterial blood has 1 volume per cent. of oxygen unsaturation and that of the mixed venous blood is 6 volumes per cent., it follows that the normal value of this factor, which is the *oxygen-unsaturation of the blood in the capillaries*, is the mean of these two, namely, 3.5 volumes per cent. (See Fig. 45d.)

4. A fourth factor, which these authors believe cannot of itself produce oxygen-unsaturation but is of importance in raising this to the threshold value in the presence of any of the other causes, is the total hemoglobin content (*T*). When this is very low, as in a profound anemia, cyanosis will not appear until oxygen-unsaturation has been raised far beyond its ordinary threshold value; and, conversely, when the hemoglobin is very high, as always in advanced polycythemia, a considerably lower content of reduced hemoglobin will reveal itself by the characteristic signs.

These factors are shown in graphic form in the accompanying chart, reproduced by permission here (Fig. 46), which reveals *V* and α (*alpha*) to be by far the most powerful of the four and the normal and "threshold values" of oxygen-unsaturation of each. According to this it is evident that one-third of the total venous blood must be shunted into the arterial stream before cyanosis from this cause will appear.

By a series of brilliant inductions it is further demonstrated that these factors tend to act in pairs, *T* (raised hemoglobin content) increasing the importance of *V* (deficient pulmonary oxygenation), and *D* (stasis in the capillaries), the seriousness of *alpha* (right-left or arterio-venous shunt). This last combination, α and *D* is the most suggestive, from the congenital cardiac standpoint, of all, for it reveals the reason why the most extreme form of congenital cyanosis and the most intense degree of clubbing in patients who survive infancy occur in the so-called "tetralogy of Fallot," (pulmonary stenosis with ventricular septal defect, dextroposition of the aorta and hypertrophy of the right ventricle) which is the commonest of all combinations in this type of congenital cardiacs reaching adult life. For this reason a chart showing the effect of *D* upon *alpha* in terms of capillary unsaturation is here reproduced. (Fig. 47) These four factors are capable of computation, and are used in equations to determine quantitatively the amount of the right-left or venous-arterial shunt.

The great service which Lundsgaard and van Slyke have rendered to the subject of congenital cyanosis has been the distinguishing of these essential causative factors from the subsidiary or modifying conditions and the graphic presentment of their relative threshold values and combined significance. In the light of this analysis the complex mass of clinical data heretofore accumulated have been largely resolved into the

simple proportions of their underlying elementary principles, and confusion is replaced by lucidity of thought.

Quantitative determination of the oxygen capacity and minute volume of the blood in a case of congenital cyanosis appears to have been first carried out by Haldane and Douglas in a case reported by Parkes Weber and Dorner,¹ in 1911. The patient was a man aged twenty-nine years,

FIG. 46

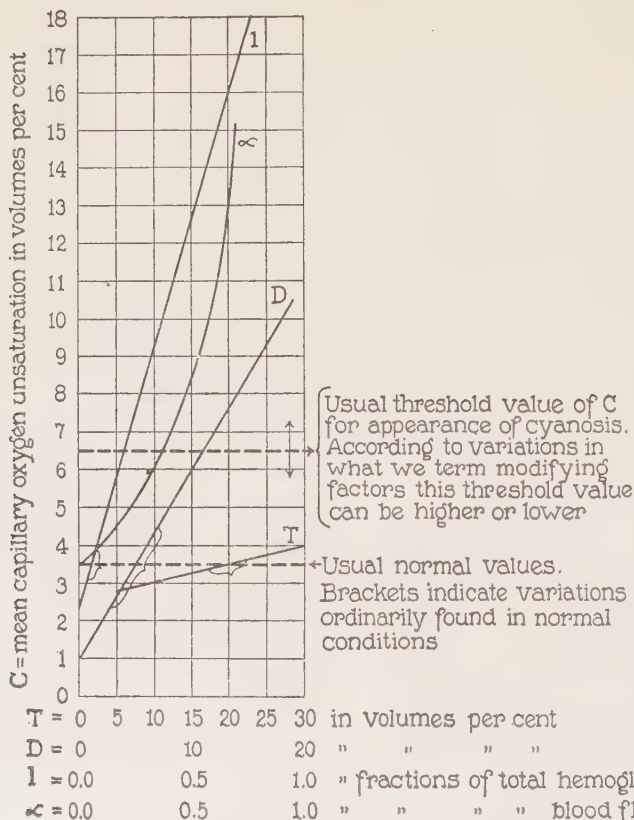


Diagram showing the relative magnitude of the influence on mean capillary oxygen unsaturation (C) of variations in total oxygen-combining power of the blood (T), in deoxidation rate during the passage of blood through the capillaries (D), in the fraction of total hemoglobin passing unoxidized through aerated parts of the lungs (l), and (α), in fraction of blood passing from right to left through channels to which air has no access. (Lundsgaard and van Slyke, *Medicine*, 1923, 2, 27.)

presenting extreme cyanosis and clubbing, with a loud systolic murmur in the second and third left interspaces, a red cell count of 10,160,00 and hemoglobin 180 per cent., blood viscosity 35.9 and specific gravity 1.086, in whom estimations made by the carbon monoxide method of Haldane and Lorrain Smith, gave 4.37 cc. oxygen capacity and 13.13 cc. volume of blood per 100 grams of body weight. These, when compared

¹ *Lancet*, London, 1911, i, 150.

with the normal values of 0.98 cc. and 4.78 cc. respectively, present an enormous increase. In the investigation made by Campbell, Hunt and Poulton of the arterial oxygen referred to above one of their patients with marked cyanosis and clubbing and an oxygen percentage saturation of 76.8 per cent. who came to autopsy showed a conus stenosis and defect of the interventricular septum above which the aorta rode receiving blood from both ventricles.

Calculation of the amount of venous blood shunted into the arterial circulation in a case shown by autopsy to be one of pulmonary atresia with septal defect and dextroposition of the aorta was attempted by

FIG. 47

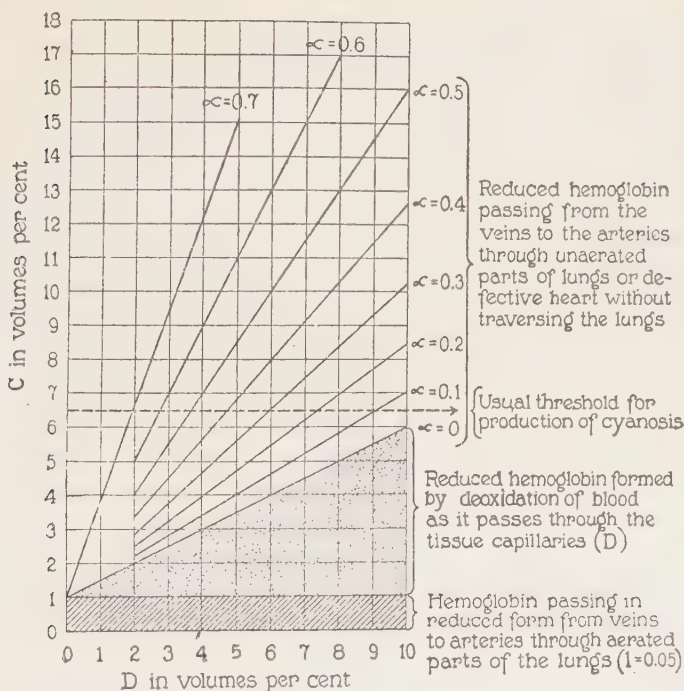


Diagram showing the influence on the mean capillary oxygen unsaturation (C) of simultaneous variations in D and α . (Lundsgaard and van Slyke, *Medicine*, 1923, 2, 32.)

Lindhard in 1922, but was not successful on account of the difficulty in obtaining the true oxygen content of the mixed venous blood. A very elaborate investigation of a similar case was made in the clinic of Prof. Biedl in Prague by Drs. Weiss and Löwbeer¹ by the method of Krogh and Lindhard. The patient was a boy, aged fifteen years, with marked cyanosis and clubbing, 8,400,000 red cells and 180 per cent. hemoglobin, who proved at autopsy to have a marked conus stenosis with ventricular septal defect and the aorta riding above and receiving blood from both left and right ventricles through this. The hemoglobin of the arterial

¹ *Wien. Arch. f. klin. Med.*, 1924, 7, 362.

blood taken by radial puncture was 75.2 per cent. saturated and had an oxygen capacity of 31.6 volumes per cent., and this, assuming that 95.5 per cent was saturated (Stadie), gave an oxygen content of 30.18 per cent. The oxygen consumption was 202 cc. per minute. From these figures the amount of blood flowing through the pulmonary veins into the right auricle (*i.e.*, the oxygenated blood from the pulmonary circulation before admixture with that of the venous shunt from the right heart), was calculated to be 2.19 litres and the oxygen content of the mixed venous blood was deduced to be 20.89 volumes per cent., while that of the arterialized blood was 23.76 volumes per cent., and from the equation thus obtained the amount of venous blood shunted into the arterial circulation was shown to be 4.89 litres, making a total volume per minute of 7.08 litres of which 2.19 litres was arterial and 4.89 litres was venous blood. This large amount of the shunt, which is nearly two-thirds of the total volume, is in accord with Lundsgaard's statement that cyanosis from a right-left shunt does not occur unless at least a third of the venous blood has been thrown into the arterial stream.

Still higher values for the degree of oxygen-unsaturation¹ and the amount of the shunt were obtained in a study carried out by Bock, Field, Stoddard and L. J. Henderson in an as yet unpublished case, kindly communicated to the writer, diagnosed as pulmonary stenosis with patent ductus arteriosus. The patient, a man aged thirty-one years, showed extreme cyanosis with great clubbing and a tendency to attacks of dizziness accompanied by unconsciousness, a red cell count varying from 7 to 12 millions, a rough systolic murmur with maximum intensity in the second left interspace with a faint systolic thrill at the same area and a faint humming murmur prolonged throughout diastole. The amount of the shunt calculated on the day when the oxygen contents was 19.74 volumes, was 74.6 per cent., which large proportion of venous blood was actually being transferred into the arterial tree! The respiratory phenomena of this remarkable case are embodied in a monograph by Dr. L. J. Henderson.²

The accompanying figure (see Fig. 48) showing the circulation in a case of tetralogy of Fallot is introduced here because this is the commonest condition underlying congenital cyanosis in adult life, so that such cases we should be able to visualize in conducting such investigation as the above. It is to be remembered always that a septal defect without pulmonary stenosis does *not* produce cyanosis, unless some other reason exists for a rise of pressure in the right ventricle or pulmonary circulation.

Variations in the Venosity of the Shunt.—The fact that patients with congenital cyanosis show a deepened blueness during muscular exertion

¹ The calculations of the amount of the venous shunt are based on the assumption that the blood leaves the lungs fully saturated, the figures used in the calculation by Weiss and Lowbeer being 95.5 per cent., and in that of Bock and Field 100 per cent. saturated. It has been pointed out to the writer by J. C. Meakins that from analogy with polycythemia vera, *we know that when the red cell count is markedly raised* (as in all advanced cases of congenital cyanosis and in the 2 cases in question) *the blood leaves the lungs under-saturated (1 factor)* owing to its concentration in the pulmonary capillaries; and this was found to be so in the case investigated by Campbell, Hunt and Poulton. It follows that the figures of the amount of the shunt in both these cases are considerably lower than calculated since the blood undoubtedly left the lungs under-saturated.

² *Comptes rendus des Séances de l'acad. des Sciences*, 1925, 180, 2066.

is explained by Haldane¹ as a physiological deepening of the oxygen unsaturation of the venous blood in general and consequently of that portion of it which is shunted into the arterial tree; as Hill and Nabarro have shown, the blood in muscle is richer in CO₂ and poorer in oxygen than elsewhere in the body, and during exercise there is a greater return of venous blood from these parts whereas with the body at rest more blood is sent to the veins from the brain and other parts rich in oxygen. Another valuable point raised by Haldane is that of the *adaptation of the body*, in subjects of congenital cyanosis, to a *lowered partial pressure of oxygen in the body tissues*, which is evidenced by the remarkable capacity

FIG. 48

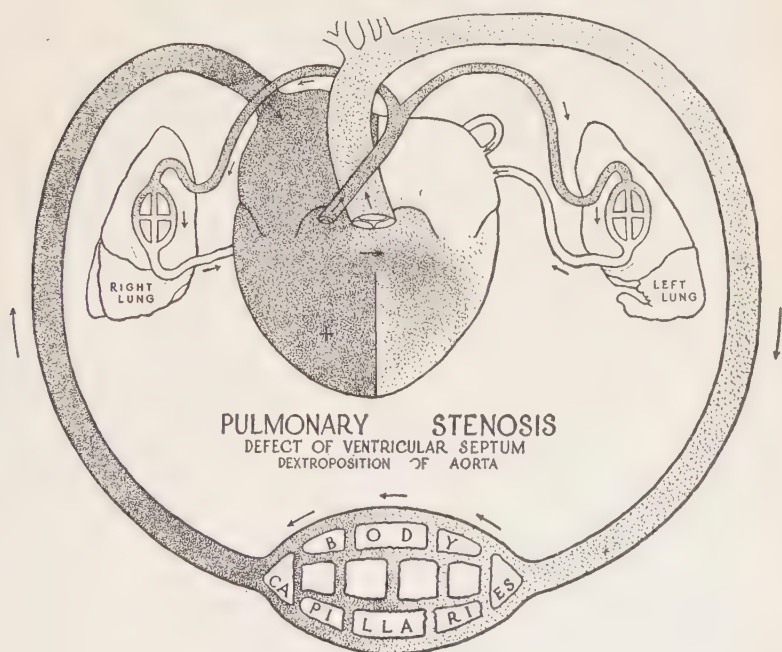


Diagram by Prof. W. T. Dawson illustrating the course of the circulation in a case of congenital cyanosis due to venous arterial shunt (tetralogy of Fallot). By courtesy of the International Clinics.

of congenital cardiacs with marked cyanosis to pursue their ordinary vocations and to undertake fairly severe muscular exertion in spite of the fact that they are undoubtedly laboring under quite a severe grade of anoxemia. Such an adaptation may be considered analogous to the gradual acclimatization of individuals to the anoxemia produced by the lowered oxygen tension of the atmosphere in high altitudes.

Symptoms.—The degree of discoloration varies from a slight bluish tinge of the cheeks and mucous membranes appearing on exertion or excitement, to a distinctly leaden hue of the whole surface, becoming purple in extreme cases. It usually increases gradually, and in many

¹ *Respiration*, Yale Press, 1922, p. 259.

cases marked at the last it is absent at birth, appearing after weeks, months, or even years, when some intercurrent event has heightened the embarrassment in the pulmonary circulation. As a general rule, the degree of cyanosis may be said to depend upon the character of the defect. Thus it is usually *slight* or *entirely absent*, *except during dyspnœic attacks*, or as a *terminal event*, in *patent foramen ovale*, *patent ductus*, or *septal defects*; a *quite moderate* degree characterizes those anomalies, such as *triloculate heart*, in which there is a free intermingling of the two blood streams, but no pulmonary obstruction; the *marked* cases which often

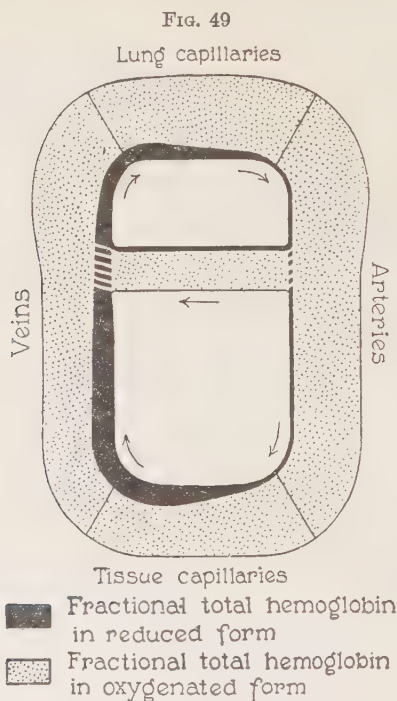


Diagram showing the proportion of oxy-hemoglobin to reduced hemoglobin in different parts of the circulatory system in a case in which a fraction of blood passes from the left side of the heart to the right through an abnormal communication. (Arterial-venous or *gamma* shunt). From Lundsgaard and van Slyke, *Medicine*, 1923, vol. 2. By permission of Williams & Wilkins.

reach early adult life and are then evident to every observer as “congenital heart disease,” occur nearly always in *pulmonary stenosis* with or without septal defect; and the most *extreme grades*—the typical “blue baby” are seen in the complete interference with the blood supply to the lungs which takes place in *pulmonary atresia* or *transposition* of the great trunks.

The subject of advanced congenital cyanosis presents a striking appearance. The superficial vessels are often dilated, the face congested, the tongue “geographical,” the eyes discolored, and sometimes bulging, the tips of the fingers, toes, and nose, flattened and bulbous, and the respirations heightened to actual dyspnœa. Traces of anasarca and

œdema sometimes occur, but form no essential part of the picture, although of course present at the close in cases which terminate with failing compensation. The temperature is usually low, especially in the extremities, and there is a tendency to catarrh, severe coughs, and colds on slight provocation. Hemorrhages, especially from the nose, and spitting of blood are prone to occur. Disturbances of eyesight, dimness of vision or even blindness, may occur from neuroretinitis.

Delayed development is frequent. In Goodman's¹ case, patent ductus arteriosus in a boy aged fourteen, this was evidenced by retarded ossification of the pisiform bone of the wrist on roentgen-ray examination (*Rotch's sign*). The patients are sometimes of very high intelligence, but when the cyanosis has set in early they are often stunted mentally as well as physically, somnolent in thought, and sluggish in action. In females the menstrual function is often delayed in onset, scanty, and irregular. In the cases with marked polycythemia, in addition to peripheral signs of venous congestion and plethora, cyclic (postural or orthostatic) albuminuria may occur. Parkes Weber records a case in a youth aged twenty-two, with great cyanosis and clubbing and a blood-count of 10,300,000 red cells, in whom repeated examination showed the early morning urine to be free from albumin, while that passed at 11 A.M., contained a considerable amount. Cyanotic patients bear the acute infections of childhood well, but frequently succumb to pulmonary tuberculosis. Another common cause of death is bronchopneumonia.

Special Symptoms.—*Clubbing and Cyanosis Retinæ.*—These symptoms constitute the visible evidences of a generalized dilatation of the smaller bloodvessels over the body surface with accompanying productive changes. New formed capillaries, arterioles with thickened walls, tortuous dilated veins, and new connective tissue formation have been observed in advanced cyanosis, both in the skin (Variat and Gampert²) and in the lungs, as well as in the retina and bulbous finger ends. The causation of these vascular and tissue changes is certainly complex but their chief source is, undoubtedly, stasis and lack of oxygenated blood, and the effect that these conditions produce upon the tissues, by means of the toxic products of metabolism which escape oxygenation.

In *clubbing* of the extremities especially, these mechanotoxic factors are at work, and lead, in extreme cases, to what resembles a congestive type of scleroderma (Buhl). This is well shown in the cases reported by Ogle,³ and by Groedel II⁴ of a huge aneurism of the subclavian artery, which, by pressing upon and obliterating the axillary artery and vein and brachial plexus (Ogle's case), led to an enormous tumefaction with intense cyanosis and clubbing, strictly confined to the arm and fingers of the affected side.

Clubbing of pulmonary or hepatic origin, and that of chronic osteoarthropathy (with proliferative changes in the shafts of the long bones), has been sharply distinguished from that of congenital cardiac disease

¹ *Amer. Jour. Med., Sci.*, 1911, **123**, 599.

² *Gaz. d. Hôp.*, vol. **13**, p. 315.

³ *Tr. Path. Soc.*, London, 1859, **10**, 103.

⁴ *München. med. Wchnschr.*, 1906, **53**, 264.

on the ground that there is in the latter cases no new formation of bone (Ebstein¹) and that the cause of the clubbing of pulmonary cases is absorption of toxins from the lung. Increased bone formation in the clubbed finger ends of the cardiac cases has been recorded, however, by Bamberger, Janeway,² Groedel II, and Miller.³ Further, a case has been reported by Batty Shaw and Cooper⁴ in which in the entire absence of pulmonary disease, signs of septal defect, with deep cyanosis, polycythemia and clubbing were combined with *thickening of the shafts of the tibia and other long bones* as well as of the clubbed terminal phalanges (x-ray examination). This indicates that in this case at least of congenital cyanosis we are dealing with a milder grade of one of the essential symptoms of Marie's disease.

The so-called hippocratic finger ends are broadened laterally and are slightly flattened, of bulbous appearance, with *distally curved nails*, (compare the more elongated finger ends and side to side convexity of the marked pulmonary cases). The nails are often shortened and without lunulæ and may be irregularly thickened from areas of vascularization or thrombotic processes in the matrix below. Microscopically, increase in the soft tissue and often in the fat (deficient aëration) is conspicuous; surprisingly little tissue change is sometimes manifest. The most striking feature, according to D. Campbell,⁵ is the thickness developing between the nail and finger-bed due to marked edema.

The invention of capillary microscopy by Lombard (1912) and Weiss (1916) and the discovery by Krogh⁶ of the constant variation and opening up of resting capillaries during activity known as the capillary motor function, followed by the really beautiful quantitative studies carried out by Krogh and his associates and followers in this subject into the size, number and variations in form of the skin capillaries in health and disease, has, within the last ten years, opened up a new chapter in the physiology of the circulatory system that is bound to throw light upon the phenomena of clubbing. So far, few direct observations have been made, the only one of which we know being that by Rominger,⁷ who inspected the capillaries at the nail-fold by the method of Weiss in a case of pulmonary stenosis and found a condition of stasis existing. The recent studies, however, by Crawford and Rosenberger,⁸ on the measurement and computation of variation in the capillaries in auricular fibrillation (circulatory stasis) and those by Brown and Sheard,⁹ into the state of the capillaries in polycythemia vera, have an indirect but none the less valuable bearing, as also those by Boas¹⁰ on the "giant capillaries" seen in the stasis of acrocyanosis. In polycythemia it is the venous part of the capillary loop that becomes most engorged and every resting capillary was seen to be called into action in Brown's investigation.

Cyanosis Retinæ sive Oculi.—Cyanosis of the retina was described and figured in Liebreich's *Atlas*, in 1863. Eighteen published cases were

¹ *Deutsch. Arch. f. klin. Med.*, 1906, p. 66.

² *Am. Jour. Med. Sci.*, 1903, **126**, 563.

³ *Trans. Am. Ped. Soc.*, 1904, **16**, 267.

⁴ *Clin. Soc. Trans.*, 1907, vol. **40**, 260.

⁵ *Brit. Med. Jour.*, 1924, i, 145.

⁶ *Yale University Press*, 1922 (gives Bibliography).

⁷ *Deutsch. Med. Wchnschr.*, 1920, **46**, 168.

⁸ *Jour. Clin. Invest.*, 1926, **2**, 365.

⁹ *Ibid.*, 1926, **2**, 1423.

¹⁰ *Jour. Am. Med. Assn.*, 1922, **79**, 1904.

collected by Posey¹ in 1905, and Holloway² has brought the number recorded to 27. Ocular changes would probably be found in nearly all cases of cyanosis if the eye grounds were examined, and this should always be done for diagnostic reasons; Babinski reported a case in which dilatation of retinal vessels preceded the appearance of cyanosis; so also Carpenter.

In this condition ophthalmoscopic examination reveals marked changes in the optic disk, congestive and secondarily inflammatory in character. The disk, itself, is unduly reddened or bluish, or sometimes hazy and swollen (neurorinitis), and is traversed by numerous previously invisible capillaries, and by greatly broadened, often tortuous veins which sometimes show a deep reflex stripe along their surface, and are filled with dark brownish or even blackish-looking blood. The arteries may share in the dilatation and violet discoloration (as in 12 out of the 27 cases recorded), or they may be quite unchanged, showing up in sharp contrast; or again, as in the cases of Baquis and Stanglomeier, they may be contracted. Retinal hemorrhages are common. The difference in the appearance of arteries and veins was suggested by Nagel as diagnostic between anomalies due to admixture of currents (septal defects, etc.), and those due to pulmonary obstruction only, the arteries in the latter case remaining unaltered. This point has yet to be substantiated by postmortem evidence.

In advanced cases the ocular changes are not confined to the disk but involve the whole eye, which bulges outward (exophthalmos) and shows marked conjunctival congestion and cyanosis. Hemorrhages may occur into the vitreous or more superficially, and rupture of the cornea (Goldzieher³), or glaucoma, from congestion of the ciliary body, may occur. Severe iridocyclitis may develop, as in the cases of Goldzieher and Baquis.⁴ In both of these the iris turned while under observation from a bright blue color to a yellowish brown, a change found by the ocular microscope to be due to extreme congestion. This symptom was the more remarkable because it was seen to disappear after death. Baquis' case was a boy aged eleven, with extreme cyanosis and clubbing, a blood count of 8,500,000 red cells and pulmonary stenosis with septal defect. He gives a careful description of the microscopic findings in the diseased eyeballs and adds a study of eight other cases in the German literature.

Dyspnœa.—Investigation of the respiration was carried out in two cases of congenital cyanosis by Rubow⁵ (1908), and in a third case by Bie and Maar⁶ (1910). They found both total, middle, and vital capacity were lowered, but that the percentage of middle to total capacity was normal, and considered that the only essential change in the cases examined by them was a marked acceleration of the respiratory rate and the resultant increase of pulmonary ventilation. Peabody⁷ in his valuable researches on cardiac dyspnœa shows that this symptom is always accom-

¹ *Am. Jour. Med. Sci.*, 1905, **130**, 415.

² *New York Med. Jour.*, 1912, **14**, 71.

³ *Centraib. f. prak. Heilkunde*, September, 1904.

⁴ *von Graef's Arch. f. Ophth.*, 1908, **51**, 68.

⁵ *Deut. Arch. f. klin. Med.*, 1908, **92**, 255.

⁶ *Ibid.*, 1910, **99**, 382.

⁷ *Harvey Lectures*, 1916-1917, **12**, 248.

panied by a high minute volume, and believes that a suggestive relationship exists between this and the fall in vital capacity, which "is the earliest and most constant feature in the production of dyspnœa." The cause of the decrease in vital capacity in cardiac cases is ascribed by him to a lessening of the respiratory surface such as occurs in atelectasis or emphysema, and by Siebeck (quoted by Peabody) to loss of elasticity in the lung tissue due to engorgement from the back pressure that occurs especially in mitral lesions. That abundant cause exists in the lungs of long-standing cases of congenital cyanosis for a lowered vital capacity both from lessening of surface and loss of elasticity is evident from the studies of Carpenter, Thomas and others. That acidosis may take part in advanced cases is suggested by the usual lowered alveolar CO₂ tension which would act through irritation of the respiratory centre.

Dyspnœa is an early and prompt feature. It usually sets in before the cyanotic color is manifest. It frequently culminates in the so-called *dyspnœic attacks*, which in their typical form and full development, are seizures of extreme respiratory distress usually attended by marked cyanosis, and sometimes by unconsciousness, in which death may take place. Such attacks are characteristic of all severe cases of congenital cyanosis and also of conditions in which there may be no trace of cyanosis except at these times. Transient cyanosis of this type has been described by Sebilléau¹ as *la cyanose paroxystique congénitale*. Respiratory failure may be evidenced also by repeated syncope or by anginal crises.

Polycythemia.—This is a common characteristic of cyanotic blood. The red cells frequently number 7,500,000 to 8,500,000, per cmm., the percentage of hemoglobin is raised, and in some cases the red cells are also increased in size. Counts of 12,750,000 are reported by Murray Leslie,² 10,000,000 by Pick, Bernstein, and Parkes Weber, and the count reached 12,000,000 in two unpublished cases within the writer's experience, those of Drs. Bock and Field and Harris MacPhedran.

The increase of the red cells is of the nature of a vital compensatory process, and is to be compared to the polycythemia of high altitudes. Weil³ describes in detail a microscopic finding in two cyanotic children with pulmonary stenosis in whom the red cells numbered respectively 7,502,000 and 8,540,000. The hematopoietic organs and also the other tissues examined were crowded with vasoformative cells and embryonic capillaries and the bone marrow showed a typical erythroblastic reaction. Similar appearances have been noted by other observers and prove that this feature is part of the compensatory mechanism of the organism for the better oxygenation of the tissues.

The blood count differs somewhat at different parts of the body and according to whether the specimen has been drawn from arteries, veins, or capillaries but it remains far above the normal, the increase in red cells remaining an absolute and not a relative quantity (Bie and Maar). That is to say the total quantity of blood in the vessels is increased, a degree of plethora existing.

¹ *Thèse de Paris*, 1895.

² *Proc. Royal Soc., Clinical Section*, 1908, 2, 34.

³ *Compt. rend. de la Soc. de biol.*, 1901, 53, 913.

Polycythemia is not a constant feature in congenital cyanosis, it is characteristic rather of the later stages of the disease, and while favorable in so far as it represents an attempt at compensation, the appearance of the red cell count above 6,000,000 points to a grave prognosis (Vaquez and Quiserne).¹

The present status of our knowledge on the polycythemia of congenital heart disease has recently been reviewed (with full bibliography), by Dr. Parkes Weber² whose own researches upon this subject make this an authoritative contribution. The name erythrocytosis is given by him to the increase of red cells, which is in these cases a conservative vital reaction, an automatic attempt on the part of the hemopoietic centres to make up for deficient oxygenation by increase in the red cells of myelogenous origin, and the viscosity of the blood is always much raised above normal as is also the specific gravity. Curious epileptiform attacks associated with coma and sometimes setting in with acute mania, as in the case of Bock and Field, and in a case of "Fallot's tetralogy" in a man, aged twenty-three years, with extreme cyanosis and clubbing under the care of Campbell P. Howard, appear to be due to a temporary thrombosis of the cerebral capillaries produced by the high degree of viscosity of the polycythemic blood.

Diagnosis.—The cyanosis of congenital cardiac disease must be differentiated from a number of other forms. Of first importance among these is the so-called enterogenous cyanosis³ (first described by Stockvis and other Dutch observers), in which the dark color of the blood is due to a sulph-hemoglobinemia or methemoglobinemia, produced, it is thought, by the action of hydrogen sulphide or other toxic agents upon the blood. Again, certain aniline poisons lead to a methemoglobinemia giving a dark discoloration to the skin, and polycythemia with splenomegaly is sometimes, although not always, associated with cyanosis. These conditions differ from congenital cyanosis in the slightly different tinge of the skin, which in methemoglobinemia is of a grayish hue, in polycythemia with splenomegaly of a more florid aspect, by the absence of cardiac signs, by the presence of intestinal symptoms, and by the history of a toxic factor or the presence of enlargement in spleen and liver. In methemoglobinemia the red cells are not increased in number.

Other conditions leading to cyanosis with clubbing are pulmonary emphysema, bronchiectasis, adherent pericardium, and Ayerza's disease,⁴ in which chronic cyanosis, dyspnoea and erythrocytosis are associated with a fibrosis of terminal branches of the pulmonary artery. In all these cases the cyanosis is due to a lowered oxygenation of blood in the pulmonary alveoli (Lundsgaard's 'I' factor) and the diagnosis may be established by the fact that the cyanosis disappears on the administration of oxygen.

¹ *Compte rendu de la Soc. de biol.*, 1902, **54**, 915.

² *Polycythemia, Erythrocytosis and Erythræmia*, Paul B. Hoeber, New York, 1922.

³ A digest of enterogenous cyanosis, with a tabulated statement of the recorded cases and full bibliography, is given by West and Clarke (*Lancet*, February 2, 1907). Other important articles are by Hymans van den Bergh (*Deutsch. Archiv f. klin. Med.*, 1905), Oliver (*Lancet* December 29, 1906), Gibson (*Lancet*, July 14, 1906), and Blackader (*New York Med. Jour.*, March 16, 1907).

⁴ See article by A. S. Warthin, *Trans. Assn. Am. Phys.*, 1919, **34**, 219.

Polycythemia vera (Vaquez-Osler disease) or erythremia as it is termed by Parkes Weber, presents certain resemblances to congenital cyanosis with a secondary polycythemia, in that the patients are very easily cyanotic, and clubbing is said sometimes to occur probably owing to the increase and engorgement of the capillaries. The rubicund color and the normal condition of the heart and lungs and history of the case are sufficient guides. An interesting study of the vascular changes in this condition has just been published by Brown and Giffin.¹

THE NON-CYANOTIC GROUP OF CONGENITAL CARDIACS

From the foregoing discussion, it is evident that only a certain proportion of cases of congenital cardiac disease present the symptom-complex of congenital cyanosis, those, namely in whom the defect has led to an increased oxygen-unsaturation either by deficient aëration in the lungs (*I* factor), entrance of an anomalous current of venous blood into the arterial stream (α factor), or increased oxygen-consumption in the tissues (*D* factor). There remains a considerably larger group of cardiac anomalies of much clinical significance in whom cyanosis is either *entirely absent throughout life*, or is *present only as a terminal or transient phenomenon*. These cases, which may, for lack of a better terminology, be termed the non-cyanotic group, may be differentiated, from the anatomical and clinical standpoints, as follows:

(a) *Those in which there is no abnormal communication between the two circulations*, but in which the defect produces a mechanical interference with the circulation, which constitutes it a seat of strain, leading to failure of the left heart, atherosclerosis and sometimes rupture of the aorta, and frequently to a bacterial endocarditis or endarteritis in the vicinity of the defect, which supplies a *locus minoris resistentiæ*. Such are: bicuspid semilunar valves, coarctation of the aorta, congenital left-sided valvular lesions, etc.

(b) *Those in which an abnormal aperture of small size exists between the systemic and pulmonary circulations*, uncomplicated by other anomalies, so that the normal relative pressure of the two circulations is unchanged and, this being physiologically higher on the left or systemic side, an arterial-venous shunt of blood passes from left to right through the anomalous opening. These are the cases of localized uncomplicated defects of the cardiac septa and (with certain reservations) patent ductus arteriosus, and in these, as was shown by Bard et Curtillet for defects of the interauricular, and Reiss, Le Houx,² and others for defects of the interventricular septum, a reversal of flow may and frequently does occur from an intercurrent rise of pressure in the right heart, leading to a terminal or *transient cyanosis* (*Cyanose tardive*). In arterial-venous shunt the strain is thrown on the pulmonary circulation, and the pulmonary artery is usually much dilated, especially in auricular septal defects and patent ductus, and may be atheromatous, and is sometimes even the seat of a dissecting aneurism (Durno and Brown³); the same tendency

¹ *Am. Jour. Med. Sci.*, 1926, **171**, 157.

² *Paris Thèse*, 1902.

³ *Lancet*, London, 1908, i, 1693.

FIG. 50

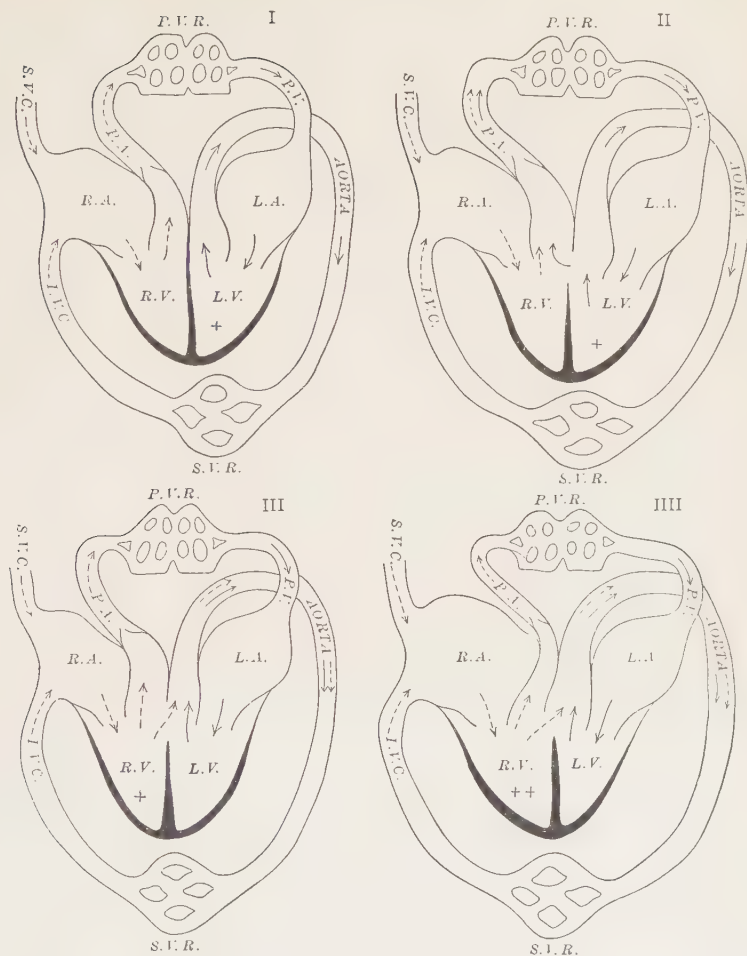


Diagram showing the effect of a raised relative pressure in the (a) left or (b) right ventricle of the heart, resulting in an (a) arterial-venous, or (b) venous-arterial shunt, which may be of functional origin, (cyanose tardive) (as in III), or a permanent organic condition of (morbus cœruleus) (as in IV). Drawing by Dr. L. Gross. P. V. R. pulmonary venous reservoir; S. V. R. systemic venous reservoir; black arrow; arterial blood shunted; dotted arrow: venous blood shunted.

I. Normal conditions of the circulation.

II. Uncomplicated localized ventricular septal defect (*Maladie de Roger*) under conditions of functional efficiency. The pressure is + in the left ventricle and a current of arterial blood (shown by the black arrow) passes from left to right through the defect. Cyanosis is absent.

III. The same ventricular septal defect in cardiac decompensation or rise of pressure in the pulmonary circulation from any cause. The pressure is + in the right ventricle and the current passes from right to left through the defect (venous arterial shunt—*cyanose tardive*.)

IV. Ventricular septal defect complicated by pulmonary stenosis and dextroposition of the aorta. The pressure is permanently raised in the right ventricle and a permanent venous-arterial shunt exists (morbus cœruleus).

also exists here as in the other "non-cyanotic" cases to the development of a bacterial endocarditis about the margins of the defect especially in that of the interventricular septum and patent ductus; moreover, there always exists here the possibility of the conversion of the relatively harmless arterial-venous shunt into a venous-arterial one.

On account of these dangers, these cases of the so-called "non-cyanotic group" both those without abnormal communications and the septal defects with arterial-venous shunt, all of whom usually reach adult or advanced life and whose "expectation" is good, should be protected from cardiac over-strain, pulmonary disease and focal infection.

The diagram on page 647 (Fig. 50) contrasts the course of the circulation through a localized defect of the interventricular septum (*Maladie de Roger*) under physiological conditions when the pressure is highest in the left ventricle, and an arterial-venous shunt is produced (Diagram II), with the altered course of the anomalous current when the pressure is raised in the right ventricle through pulmonary complications or failure of the left heart when a terminal or transient venous arterial shunt is produced (Diagram III), and with that in the *great and persistently raised* pressure that exists in the right ventricle when a ventricular septal defect is associated with a pulmonary stenosis and dextroposition of the aorta, in which condition there a constant venous-arterial shunt from birth, which places the oxygen-unsaturation of the arterial blood permanently above its threshold value and produces a true morbus cœruleus.

INCIDENCE OF BACTERIAL INFLAMMATORY PROCESSES

The importance of this subject, both on account of the grave menace which it holds for all patients with congenital cardiac disease who attain years of maturity, and also because of the contribution which it yields to our knowledge of the mode of invasion of infective processes originating at a seat of mechanical strain, makes a special reference to it necessary here. The cardiac anomalies of the "non-cyanotic type," especially bicuspid semilunar valves, defects of the upper part of the interventricular septum (*Maladie de Roger*), and patent ductus arteriosus, are most frequently the site of infective processes, and also those milder cases of congenital cyanosis who reach adult years, *i. e.*, pulmonary stenosis. The reason that the more complex and serious defects, such as transposition of the great trunks, persistent truncus, biloculate heart, pulmonary, mitral and tricuspid atresia, etc., usually appear to escape, is undoubtedly because these grave anomalies lead to an extreme degree of oxygen-unsaturation, and death occurs in infancy or early childhood before the age at which a bacterial infection is likely to supervene.

A statistical analysis of the 656 cardiac anomalies of clinical significance in the writer's series of 850 cases charted, shows several points of interest in this regard. Among these 656 cases there were 395 of the non-cyanotic, and 261 of the cyanotic type, and the total incidence of acute endocarditis was 129 cases making 19.6 per cent., of which 90 cases were in the non-cyanotic, and 39 in the cyanotic group.

The relative frequency in the different lesions of the *non-cyanotic* group was as follows: In fused semilunar cusps, 11 times in 31 cases (35.5 per cent.); in defects at the *upper part* of the interventricular septum, 22 times in 54 cases (41 per cent.); in defects at the *lower part* of the interventricular septum (persistent ostium primum) 3 times in 15 cases (20 per cent.); in patent ductus arteriosus, 23 times in 84 cases (27.3 per cent.), or, deducting the 20 cases of patent ductus in children under four years, 23 times in 64 adult cases (35.9 per cent.), in communication between the aorta and pulmonary or base of right ventricle (aortic septal defect), 4 times in 21 cases (18 per cent.); and at the seat of the stricture in coarctation of the aorta 12 times in 60 cases (20 per cent.).

In sharp contrast to the above is the fact *that* infective endocarditis did *not* occur in the vicinity of the defect in any of the 32 cases of uncomplicated patent foramen ovale nor in 9 other defects at the *upper part* of the interauricular septum; nor did it involve the margins of a defect in the *lower part* of the interventricular septum, *i. e.*, when this lay at a distance from the auriculo-ventricular cusps. The inference is clear that the neighborhood of the valvular endocardium is an important predisposing cause, as is also the location of defect in the arterial wall, which is apparently equally susceptible; this is shown by the high incidence of bacterial endocarditis in patent ductus, in which case the *pulmonary* end of the ductus and wall of the pulmonary artery adjacent is the seat of election, first becoming involved.

Of the 261 cases of the cyanotic group analyzed, 96 were cases of pulmonary stenosis (usually with associated septal defect), and among these acute endocarditis occurred in 26 (27 per cent.). Among the remaining 167 cases of this group, which were mostly cases of extreme morbus cœruleus in mitral, aortic, tricuspid, or pulmonary atresia, transposition of the great trunks, etc., dying in early life, an infective process was present in only 10, which is an incidence of only 0.06 per cent.

A very interesting literature exists upon this subject, which early attracted the attention of clinicians. The first mention of an acute inflammatory process, involving a *valvular anomaly*, appears to have been made by Sir James Paget (1844), who described a luxuriantly vegetative growth which filled the pulmonary artery to its bifurcation and originated on the surface of a congenitally bicuspid pulmonary valve, in a girl, aged twenty years, who had a gonorrhœa. He commented as follows: "I believe it has never yet been noted, though there can be no doubt about the fact, that in the majority of cases in which only two valves have been present in the aorta or pulmonary artery, these valves have been diseased, and often extremely diseased." Peacock remarked similarly on the frequency of an acute endocarditis both in septal defect and in bicuspid valves. Osler in 1880 wrote: "This condition (bicuspid valve), is a very dangerous one from the special liability of the combined curtain to disease," and later (1886), he tabulated 18 personal cases of bicuspid aortic valve (see Fig. 85, page 749), in 8 of which ulcerative endocarditis had occurred. Garrod in 1897 reported a case of malignant endocarditis on a congenitally bicuspid aortic valve due to a pneumo-

coccus infection secondary to otitis media. Parkes Weber¹ (1899) also drew attention to the frequency of infective processes in this anomaly. Lewis and Grant demonstrated that the subacute infective process present in 8 cases of congenital fusion of the aortic cusps in their series, had attacked the weakened inner coat of the aorta at an area of sclerosis or from a crevice in the valvular deformity, *which had thus acted as a trap or nidus* for the lodgment and accumulation of bacteria circulating in the blood stream, thus favoring the development of a vegetative process which spreads by contiguity, often with a rapidity in marked contrast to the relatively innocuous character of the causative organisms. A similar intimal origin of the infections was observed in the cases of patent ductus arteriosus with acute infective pulmonary endarteritis studied by Hamilton and Abbott (1915) and by Schlaepfer² (1926). The luxuriant vegetations in the pulmonary artery in the instances of communication between the systemic and pulmonary circulation have been illustrated in various reports. Boldero and Bedford suggested that the rich growth of vegetations might be caused by the presence of the more highly oxygenated blood thrown into the pulmonary circulation by the arterial-venous shunt through the defect. An interesting case in point is a specimen in the McGill museum in which a huge mass of firm vegetations occupied the main trunk of the dilated pulmonary artery, having sprung from a large mycotic aneurism of the wall beside the pulmonary mouth of the ductus, which was patent at this end but obliterated in its middle; a widely gaping foramen ovale, the size of a quarter dollar occupied the upper part of the interauricular septum and had permitted the passage of a large arterial-venous shunt, which may have favored the growth. A similar extraordinarily luxuriant growth in the pulmonary occurred in a case reported by Moschowitz in a defect of the interventricular septum with dextroposition of the aorta and pulmonary stenosis and in a similar condition observed by Callender and reported and figured by Abbott.³ In opposition to this suggestion, however, must be mentioned such cases as that reported by Paget, and an unpublished one under the care of Rabinovitch, in which massive vegetations of an acute pulmonary endarteritis occurred without any septal communication. In all these cases of vegetative pulmonary endarteritis multiple infarction of the lung of embolic origin was a prominent feature.

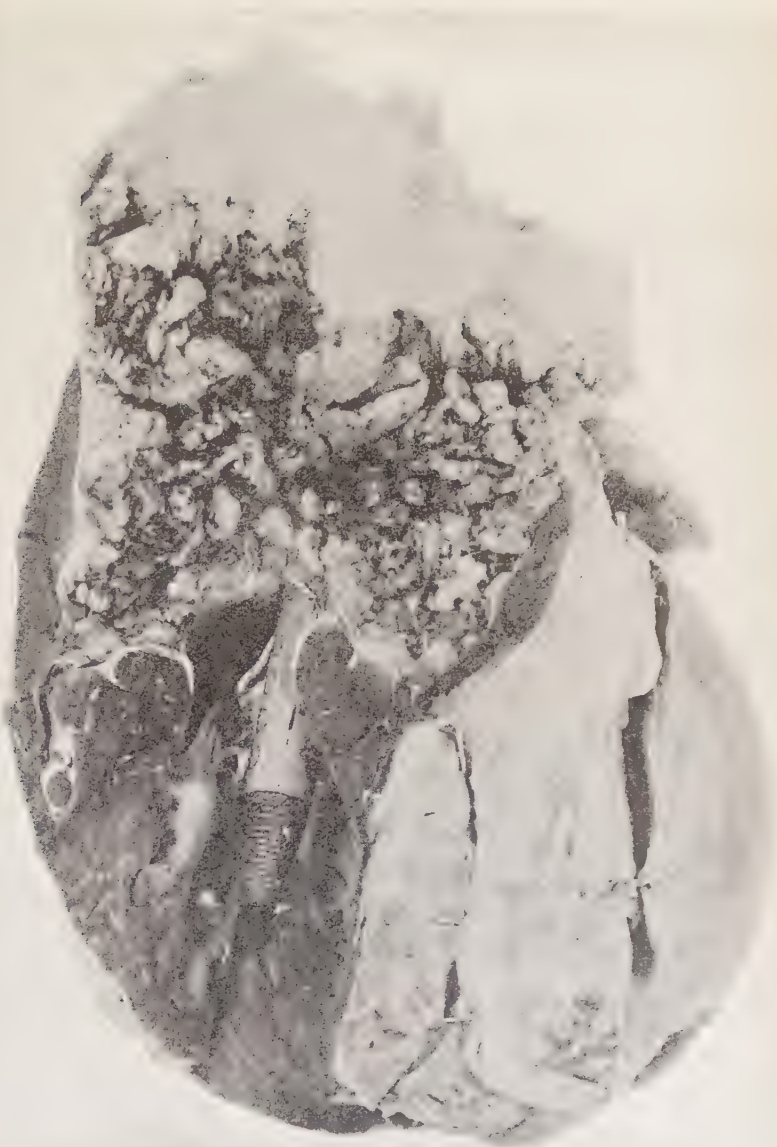
The first cases of infective endocarditis involving the margins of *ventricular septal defects* were reported by Dalrymple (1847) and Whitley (1857). An interesting feature shown in the early cases by Callender, Hebb, Tuckwell and Horder is the localization of a patch of vegetations on the wall of the right ventricle opposite the defect, produced by the impact of current from the arterial-venous shunt, which is thus demonstrated to have occurred. In 1905 Canby Robinson first called attention to the frequent termination of pulmonary stenosis by infective endocar-

¹ *St. Bartholomew's Hosp. Repts.*, 1899, **35**, 150.

² *Arch. Int. Med.*, 1926, vol. 37.

³ *Annals Clin. Med.*, 1925, **1**, 189 (bibliography).

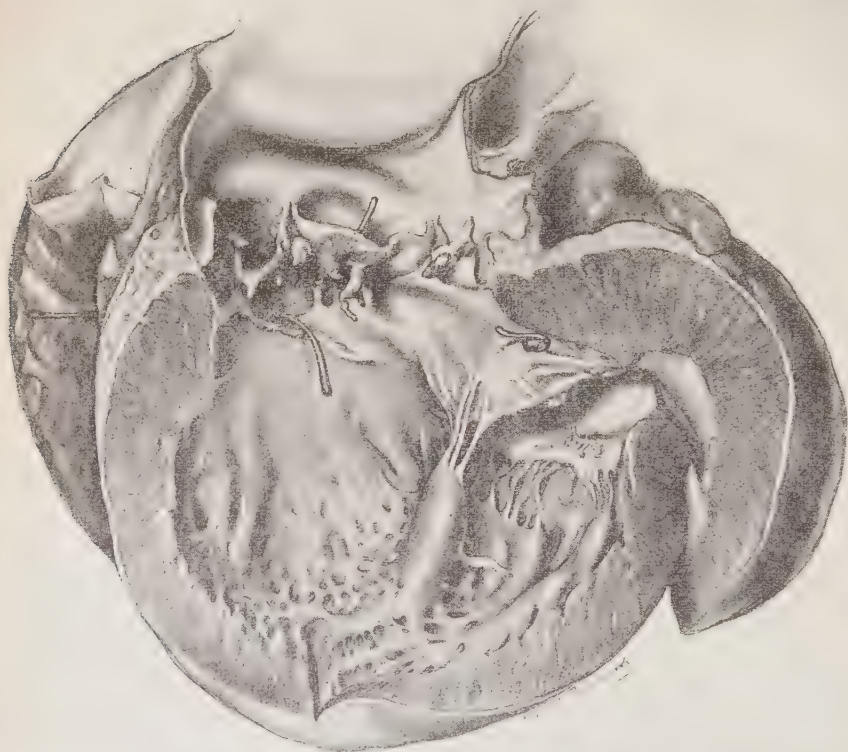
FIG. 51



Subacute bacterial endocarditis forming massive vegetations filling conus of right ventricle, destroying pulmonary cusps, invading base of pulmonary artery and occluding its lumen. Marked simple hypertrophy of right ventricle below conus, which is dilated to form a separate chamber. Defect of interventricular septum, demonstrated in this view by a rod which has been passed through the defect from the (dextroposed) aorta and emerges here in the sinus of the R. V. Male, aged twenty-one years. Cyanosis and dyspnoea and *Streptococcus viridans* in blood culture. (Major G. R. Callender, Army Medical Museum, Washington, D. C. and Prof. Laborio Gomez, University of the Philippines.)

ditis and reported 2 cases, with associated septal defect. In 1908 Sir Thomas Horder added 3 important cases, 2 of septal defects with *Streptococcus viridans* infection and one of patent ductus arteriosus with pneumococcus infection. Infective endocarditis complicating defects of the aortic septum (ruptured congenital aneurism of the right aortic sinus of Val-

FIG. 52



Subacute bacterial endocarditis (recurrent on healed lesion) involving aortic and mitral valves and margins of a large defect at upper part of interventricular septum at apex of (congenital) aneurism bulging toward right ventricle. Dextroposition of aorta, which looks into both ventricles above the defect. Subaortic fibrous band. Inflammatory perforation of right posterior aortic cusp and aortic segment of mitral. View showing interior of left chambers. From a man, aged thirty-five years. *Streptococcus viridans* in blood stream and in vegetations. Old and recent embolic lesions in kidneys. (Case of Dr. E. Libman reported by M. E. Abbott, *Annals Clin. Med.*, 1925, 4, 197.

salva) has been reported by Hart (1905) and by Abbott (1919) (*vide infra*); in the latter's case the same great redundancy of growth of vegetations in the pulmonary conus was evident.

As pointed out by Libman the infective process is usually of the subacute or "chronic infectious" form and this is particularly true of the left-

sided lesions especially bicuspid aortic valves as is well illustrated by the series by Lewis and Grant, which all showed healed or healing lesions of this form, and Osler's cases appear to have been mostly of this type. In the admirably worked-out case by Schlaepfer of acute pulmonary endarteritis in patent ductus, the *Streptococcus viridans* was present in blood cultures throughout the acute stage of the disease. Libman's case of ventricular septal defect and dextroposition of the aorta ran a typical course of repeated healing stages alternating with exacerbations, presented the usual embolic and glomerular lesions, and the *Streptococcus viridans* was present in the blood stream. (See Fig. 52.)

For some reason not at present clear, however, a greater proportion of the cases of inflammatory processes involving the right heart and pulmonary artery in ventricular septal defect and patent ductus appear to be of the *acute* infective type and due, not to the anhemolytic streptococcus, but to the pneumococcus, gonococcus, or other microorganism of high virulence, and the course is the fulminating one of a malignant septicemia.

CLINICAL CLASSIFICATION OF DEFECTS

Many attempts have been made to reduce cardiac anomalies to a scientific classification but none have been entirely successful. To the earlier workers the most logical arrangement appeared to be one based on the etiology of the defect, whether inflammatory, or developmental, and, in the latter case, on the stage at which the arrest of growth underlying the anomaly had occurred. Such a grouping, however, even supposing that the necessary data could be obtained in all cases, is of little use for the practical purposes of clinical medicine, which seeks to assemble together, as disease entities, conditions of like clinical aspects and pathological findings, whose divergence from the normal is the result of interference with definite structural principles and physiological laws. This, which is the nosography of disease, is as essential here for clear thinking as in any other chapter of internal medicine. The differentiation of "left-sided valvular lesions" (Parkes Weber) and "right-sided valvular lesions" (Newton Pitt), and the order followed by Laubry and Pezzi in their brilliant clinico-pathological treatise, are contributions along these lines. Bamberger, in 1857, proposed the grouping of cardiac anomalies as "cyanotic" or "non-cyanotic," according to the direction of the shunt and the presence or absence of an abnormal communication between the two circulations. This has been followed by Abbott and Dawson in their "Clinical Classification" (*loc. cit.*, page 8, 9 or 10), in which the course of the circulation in the different defects is diagrammatically portrayed and the cases are grouped according to the absence or presence of the shunt and its direction. In a statistical analysis of 850 cases the sequence followed has been that of the *anatomical arrangement*, and this order has been made to serve also as an index for the contents of this article. On that account the various anomalies enumerated in the chart (pages 654, 655) are listed here again, grouped on the principle of the pathological physiology of the circulation in the defect and its clinical significance on page 656.

CLINICAL CLASSIFICATION

A. *Cases of no clinical significance:* Diverticulum of pericardium; bifid apex of heart; diverticulum of heart; acardia; ectopia cordis pectoralis (non-viable); congenital rhabdomyoma; true (mirror-picture) dextrocardia.

B. *Of clinical significance.*

I. *Non-cyanotic Group.*

1. Cases in which no abnormal communication exists but in which the defect may produce a *mechanical interference* with the circulation which become the seat of strain. These are: pericardial defect; ectopia cordis abdominalis; primary congenital hypertrophy; congenital heart-block; anomalous septa; pulmonary and tricuspid insufficiency; aortic and mitral stenosis; anomalies of semilunar and auriculo-ventricular cusps; coarctation and hypoplasia of the aorta; anomalies of the aortic arch; anomalies of coronary arteries; congenital arterio-venous aneurism; certain anomalies of veins and anomalies of pulmonary artery.

2. (a) Cases of *arterial-venous shunt* with possible terminal or transient reversal of flow (*cyanose tardive*): (a) Defects of the interauricular septum (persistent ostium primum; persistent ostium secundum; patent foramen ovale); multiple defects; complete defect, (cor-biventriculare triloculare).

(b) Localized defects at the base of the interventricular septum (*Maladie de Roger*; defects below; multiple).

(c) Patent ductus arteriosus and localized defects of aortic septum (communication just above the aortic valve; congenital aneurism of the right aortic sinus of Valsalva).

II. *Cyanotic Group.* (*Morbus caeruleus*).

1. Cases of venous-arterial shunt (arranged in order of severity of shunt).

(a) *Moderate cyanosis.* Dextroposition of aorta with defect at base of ventricular septum; complete absence of ventricular septum (cor biatriatrium triloculare); pulmonary stenosis of inflammatory type with closed ventricular septum and patent foramen ovale; tricuspid atresia with interauricular septal defect and transposition of the great trunks.

(b) *Marked cyanosis:* Pulmonary stenosis with dextroposition of aorta and interventricular septal defect (tetralogy of Fallot); pulmonary atresia with ventricular septal defect, dextroposition of the aorta, and patent ductus; transposition of arterial trunks with ventricular septal defects and dextroposition of the aorta.

(c) *Extreme cyanosis:* Complete absence of cardiac septa (cor biloculare); complete defect of aortic septum (persistent truncus); transposition of arterial trunks with patent foramen ovale and patent ductus but closed interventricular septum; pulmonary atresia with closed ventricular septum, patent foramen ovale and patent ductus; aortic and mitral atresia with defect of interventricular septum and aplasia of aorta.

2. *Cases of raised peripheral pressure. Right-sided valvular lesions* with closed septa (pulmonary and tricuspid stenosis).

The 850 cardiac defects here studied present, either as the primary lesion or as a complicating condition, illustrations of practically all the

cardiac anomalies known. In the tables¹ of relative frequency, age, sex, and incidence of special symptoms and associated pathological findings, causes of death etc., the titles are grouped under a classification based on strictly anatomical principles in an order which is also that followed in the presentation of subjects in this article. Conditions "of clinical significance" are indicated in the chart by printing these in heavier type than those of purely morphological interest. A subgrouping in the case of localized defects of the interventricular septum according to the presence or absence of dextroposition of the aorta, and in the case of pulmonary stenoses, and transposition of the arterial trunks, according to the presence or absence of an interventricular septal defect, has been carried out, because these complications have a direct bearing on the symptomatology and duration of life in these conditions. The column showing the "mean" or average age of the cases studied is of great interest in these and certain other groups of clinical significance, but is introduced in the case of abnormalities of purely anatomical interest for the sake of uniformity.

The majority of cardiac defects are complicated, and it is often difficult, sometimes impossible, to say which is the primary lesion; many of the cases present other anomalies of equal importance with those with which they are grouped. A cross-index has therefore been made in the two columns next to the end, and the total relative frequency is to be found in the last column of the chart.

PART II

THE DIFFERENT DEFECTS

ANOMALIES OF THE PERICARDIUM

Absence or Defect.—The pericardium may be entirely *absent*, as in some forms of ectopia cordis, or its parietal layer may be more or less *defective*. Some forty-two cases are on record and the subject has recently been reviewed by Ebstein,² Plaut,³ McGarry,⁴ and Cameron.⁵ The defect always involves the *left* side of the sac but it may vary from a localized hole with smooth edges lying over the pulmonary artery opposite the root of the left lung and communicating with the left pleura, to complete absence of the parietal layer, the heart lying in the anterior mediastinum,

¹ NOTE.—"Double" indicates a systolic with a diastolic murmur, continuous, one which lasts throughout the cardiac cycle. The sex is not always mentioned in the records of cases. The numbers in these columns do not, therefore, always correspond to the totals in the chart. The data given as to age, sex, postmortem findings, and clinical aspects refer to the cases in the first column in the chart. This column is repeated in the third to last column, and this, added to the second to last column, gives the total relative frequency of each defect, whether classified as primary lesion or as complicating other defects.

² *München. med. Wchnschr.*, 1910, **57**, 522.

³ *Frankf. Zeitsch. f. Path.*, 1913, **12**, 141.

⁴ *Anat. Record*, 1914, February 20.

⁵ *Trans. Chicago Path. Soc.*, 1914, **9**, p. 148.

without any serous envelope. In all the cases recorded except the four above mentioned, the whole left and anterior walls of the pericardium are wanting, and the heart and left lung lie in a common cavity, the left pleura being continuous with the epicardium and the anterior and right walls of the sac being represented by one or more rudimentary folds; in the best developed cases two folds, one sagittal and one crescentic; spring from the diaphragm and are inserted, the one into the anterior mediastinum and the other posteriorly at or near the root of the left lung; in the more extreme cases the diaphragm is free and a serous fold encircles the base of the heart with the great trunks; in complete defects no trace of the parietal layer may exist, or it may be represented by a few fatty appendices arranged fringe-like about the base of the heart. The left phrenic nerve maintains its relationship to the pleuro-pericardial septum, running down parallel to the border of the sagittal rudimentary fold when this is present, and is displaced to the right in a degree increasing with the degree of the defect. This anomaly in the course of the nerve, and the serous investment of the margins of the defect, are points diagnostic of its congenital origin.

Pathogenesis.—An explanation of the condition is to be sought toward the end of the fifth week of fetal life, when the pericardial begins to be separated from the pleural cœlom. At this time the so-called pulmonary ridge, an elevation from the walls of the ducts of Cuvier, encircles, and gradually obliterates, the canal of communication between the two cavities, and descends to the septum transversum or primitive diaphragm as the pleuropericardial septum. Under normal conditions the left duct of Cuvier atrophies in early fetal life. Pericardial defect, with its invariable relation to the left pleural cavity, may well be due, as suggested by Perna, to a too early atrophy of this structure, dependent upon some anomaly of circulation in the great venous trunks, the arrested development of the pulmonary ridge resulting leading to a localized defect (pleuropericardial foramen), or to the more or less complete absence of the pleuropericardial septum. In one of Keith's cases, a defect of the left pleuroperitoneal membrane is also to be concluded, for the heart, left lung, liver, spleen, and stomach lay in the left pleuropericardial cavity.

Clinical Aspects.—The defect in itself has no direct effect upon the heart, the patients reaching adult life, and sometimes even attaining advanced age without any untoward sign. Its *clinical significance* depends chiefly upon two factors: First of these is the abnormal juxtaposition of the heart and left lung, whereby the heart is exposed, without the protection of its serous envelope, to the many inflammatory changes prone to attack the pleura; some cause also, whether traction from adhesions with the constantly pulsating heart or friction with the surface of this, appears to act deleteriously upon the left lung and pleura, predisposing these to disease. Among the forty cases recorded the incidence of left-sided pulmonary complications is extremely large. Picchi's two patients died of left lobar pneumonia, Weisbach's of left purulent pleurisy, Powell's of left pneumothorax, Plaut's second case and Faber's of acute left-sided pleurisy and Baly's, Hughes', and Saxer's of pulmonary tuberculosis.

Secondly, the *cor mobile* resulting from the lack of pericardial attachment to the diaphragm and mediastinal structures, may lead to sudden kinking of the great vessels resulting not only in symptoms of precordial distress (Ebstein), but apparently, in one instance at least in death itself. In the case recorded by Boxall death occurred on the third day after confinement, apparently from the sudden slipping of the heart's apex out of a low-walled pouch formed by two rudimentary folds attached to the diaphragm, in the altered intrathoracic pressure following delivery. Thirty hours before death urgent dyspnoea, collapse, and a systolic murmur over the precordium suddenly appeared. Pulmonary thrombosis was suspected, but was not confirmed at autopsy, when the heart was found in the left pleura. The number of fatalities is high.

Diagnosis.—This is difficult, but does not seem impossible. The greatly increased mobility of the heart, its occasional hypertrophy either from this cause or from the traction of inflammatory fibrous tissue bands attaching it to the left pleura and diaphragm, and its frequent displacement to the left through such traction or from similar causes are the chief points. In spite of its rarity, pericardial defect should always be considered in the light of the x-ray findings.

In Faber's case, a man of fifty-one years, in good health until five weeks before death, when an extensive left pleural effusion developed, the heart was only moderately displaced to the right before aspiration, although the left chest was entirely dull; after the withdrawal of 2200 cc. of fluid the apex was evident in the third and fourth interspaces in the left anterior axillary line, and at a later aspiration of 3100 cc., the heart was felt in this region by the aspirating trocar. These facts supplied a basis for a correct diagnosis.

Unattached Pericardium.—Turner describes an adult male subject in whom the parietal pericardium was perfectly free from continuity with the central tendon of the diaphragm or other structure, and was attached only about the base of the great vessels, closely embracing the heart, which could be drawn completely out of the chest (*cor mobile*), the inferior vena cava lay free in the thorax for an inch before piercing the pericardium. A similar condition was observed in the walrus and was thought here to be normal.

Diverticulum or Hernia Pericardii.—This consists in a localized bulging of the serous, or serous and fibrous, coats of the parietal layer, whereby a thin-walled cyst is formed, communicating with the pericardial cavity either directly by a narrow orifice, or by a tubular canal. An interesting example was seen by the writer in the Museum at Bologna, from a case published by Coen.¹ In this specimen a unilocular chamber of a capacity of 40 cc., formed by the protrusion of the serosa, projected from the right border of the parietal pericardium, as a kidney shaped tumor 17.5 cm. in circumference, and communicated with the interior of the pericardial sac by a minute orifice lying at the bottom of a small fossa. Coen gives an analysis of ten other cases in the literature.

This condition is of little clinical importance, usually remaining

¹ *Bull. della Soc. Med. Chi. di Bologna*, 1885, 15, Fasc. 1.

latent. Secondary pathological changes, such as calcification or fibrosis of the cyst walls, or occlusion of its orifice and consequent distention of its cavity may supervene, and make it an impediment to the heart's action. The possibility of a pericardial diverticulum should not be overlooked in the diagnosis of mediastinal tumors.

DISPLACEMENTS OF THE HEART

Ectopia Cordis.—By this term is understood a displacement so that the heart passes out of the thorax, and comes to lie either upon the outer surface of the body or in the abdominal cavity. Full bibliographical studies, with reports of cases, are given by Jones,¹ and by Ellis,² and recently by Cosgrove and St. George³ (cervical heart). Ellis, following Rauchfuss, recognizes three forms, (1) *cervical* heart, in which the organ lies high up in the neck; (2) *pectoral* heart with fissure of the sternum, and (3) *abdominal* heart in which the heart is projected through a defect in the diaphragm into the abdominal cavity.

The existence of cervical heart, or of pectoral heart with fissure of the upper part of the sternum and absence of pericardium, is not compatible with life; but in pectoral heart with inferior sternal fissure and pericardium present, it might with due care be prolonged. In Goode's⁴ patient with fissure of the sternum below the manubrium, the heart was oiled every three hours and kept covered by a cardboard box, and the child did very well for a time. In the case of pectoral heart reported by Cutler and Wilens⁵ an attempt was made on the second day to make space within the thorax by dissection, but death followed at eighty-three hours, and in that by Lannelongue (quoted by Ellis), the child lived sixteen days, dying after an attempt to suture the skin over the protruding organ. In abdominal heart on the other hand life is not necessarily shortened (witness Deschamps' case of a healthy soldier whose heart occupied the position of the left kidney in the lumbar region), and in Holtz's⁶ observation of an otherwise well-developed child, seen at age of five months, the heart formed part of the contents of an umbilical hernia which was readily returned into the abdomen. In the remarkable case reported by Holmes⁷ from Dr. Howland's service of a child, aged fifteen months dying of empyema, the bulk of the heart occupied its normal position in the thorax, but the left ventricle was elongated and displaced downward, forming a vigorously pulsating tumor which extended from the lower end of the sternum to the umbilicus. There was a large interventricular septal defect and cyanosis on crying, but life might have been indefinitely prolonged.

Dextrocardia.—This term is applied clinically to all cases in which the heart is found displaced to the right side of the thorax. Pathologically

¹ *Trans. Path. Soc.*, London, 1869, vol. 20.

² *Proc. Path. Soc.*, Philadelphia, 1906, p. 36.

³ *Am. Jour. Dis. Child.*, 1924, 27, 594.

⁴ *Virginia Med. Semi-Monthly*, 1904, p. 555.

⁵ *Am. Jour. Dis. Child.*, 1925, 30, 76.

⁶ *Med. News*, Philadelphia, 1897, 71, 769.

⁷ *Johns Hopkins Hosp. Repts.*, 1917, 18, 287.

three conditions must be distinguished. In one the heart is simply displaced to the right as a result, usually, of acquired disease (*dextro-versio cordis*); this subject has been ably discussed by Stone.¹ In the other forms (*dextrocardia proper*), the organ is congenitally altered in its position in the thorax, so that the heart not only lies to the right of the median line, but *the apex comes to point to the right*. In these latter cases two forms must again be recognized:

(a) The heart is not transposed, but appears to have undergone a simple rotation from left to right on its vertical axis, so that its left chambers come to lie more anteriorly and its right chambers more posteriorly. The apex points to the right but is formed not of the left but of the right (venous) ventricle, which remains on the right side and receives blood from the right (venous) auricle into which the venæ cavæ empty. This, which is not a true transposition, is the condition present in the majority of the cases of congenital *dextrocardia without situs inversus*. In these cases the heart is usually the seat of grave associated anomalies. This is well illustrated by Grunmach's² case. (See Fig. 53.)

(b) The heart may be completely reversed upon itself, those parts normally upon the left coming to lie on the right side, but the relation of the various structures to each other remaining unchanged, so that a complete mirror picture of the normal heart results. Here the apex, pointing to the right, is formed of what was normally the left ventricle, which now lies on the right side and communicates with the right (normally left) auricle which receives the pulmonary veins and is structurally the systemic auricle. In complete *situs inversus* this "mirror" condition is the rule, but true transposition of the heart only, without *situs inversus* is exceedingly rare, the only cases we know of on record being these of Graanboom and Rokitansky,³ one reported by Lubs⁴ and two mentioned by von Bamberger.

The etiology of these two types of congenital *dextrocardia* differs widely. Nagel⁵ reviews 6 cases with clinical and autopsy reports in the literature, and demonstrates, with the aid of diagrams, that 5 of these, namely, those by Grunmach, Geipel, Löwenthal, Barnwerth and himself, belong to the type *a* above, in which the heart is not transposed, but presents simply a persistence of the embryonic stage, in which the heart lay more to the right and its apex was formed by the right half of the common ventricle. In all five of these cases grave anomalies of pulmonary stenosis and septal defects were associated.

In the sixth case, on the other hand, that by Graanboom, in which there was mirror-picture transposition of the heart, and the septum was entire, the probable explanation is to be sought, not in an arrest of development, but, with the causes of heterotaxy in general, in an altered relation of the embryo to the primitive chorionic villi. *Dextrocardia* of this type *b without* inversion of the other viscera is commonly the seat also of irregularities in development, and such complex cases can only be

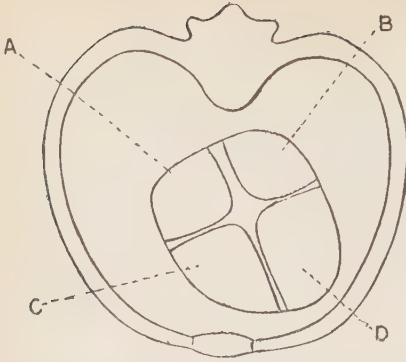
¹ *Boston Med. and Surg. Jour.*, 1904, **150**, 29.

² *Berlin. klin. Wchnschr.*, 1890, **27**, 22.

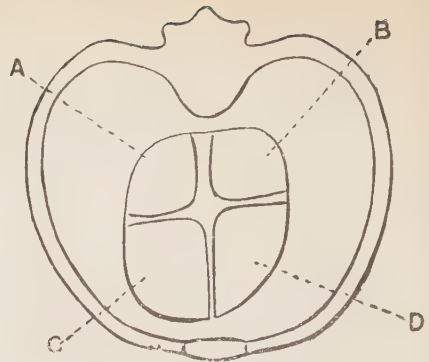
³ *Zeitschr. f. klin. Med.*, 1891, Bd. 18, 2.

⁴ *Kiel Thésis*, 1911.

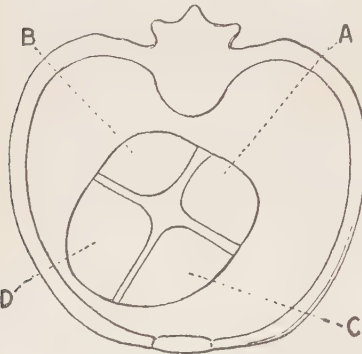
⁵ *Deut. Arch. f. klin. Med.*, vol. **96**, p. 552.



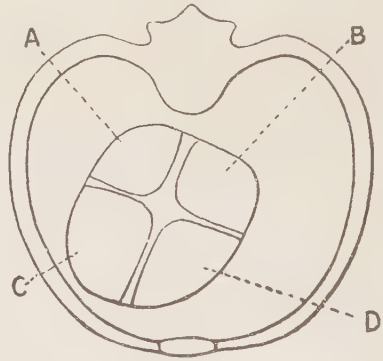
1. Normal heart. A, caval auricle; B, pulmonary veins auricle; C, right ventricle (caval blood ventricle); D, left ventricle (pulmonary blood ventricle).



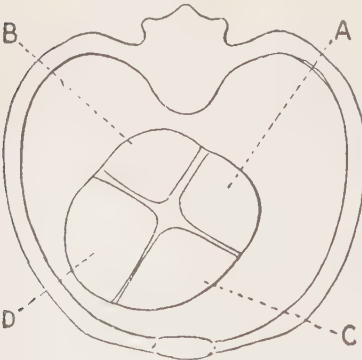
2. Embryonic heart. A, caval auricle; B, pulmonary veins auricle; C, right ventricle (caval blood ventricle); D, left ventricle (pulmonary blood ventricle).



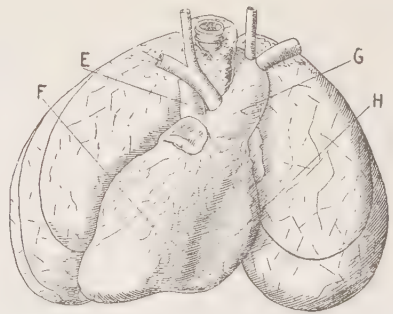
3. Mirror picture of normal heart. A, caval auricle; B, pulmonary veins auricle; C, right ventricle (caval blood ventricle); D, left ventricle (pulmonary blood ventricle).



4. Pure congenital dextrocardia. A, caval auricle; B, pulmonary veins auricle; C, caval blood ventricle; D, pulmonary blood ventricle. Note similarity to No. 2.



5. Graanboom's case of congenital dextrocardia (mirror picture). A, caval auricle; B, pulmonary blood ventricle; C, caval blood ventricle; D, pulmonary blood ventricle.

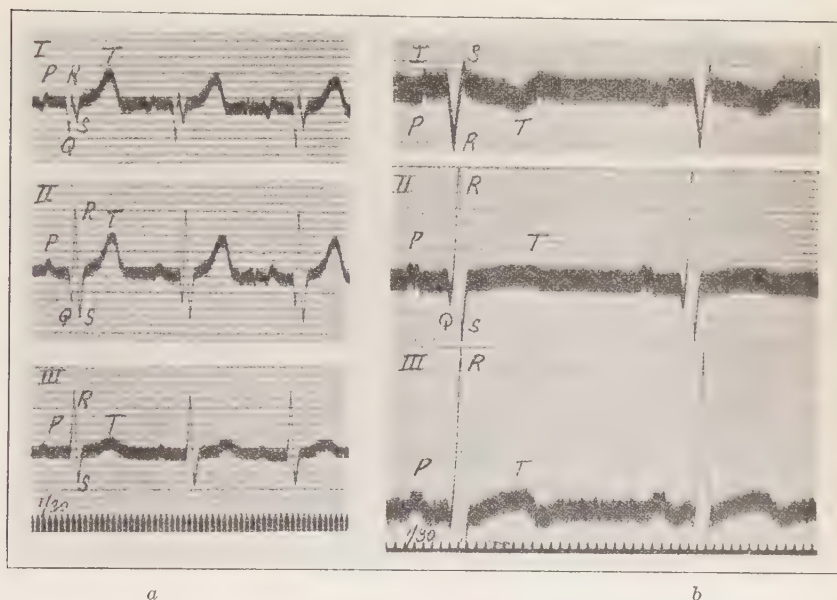


6. Grunmach's case of pure congenital dextrocardia (arrest in embryonic stage). E, vena cava superior; F, ventriculum dextrum; G, aorta; H, ventriculum sinistrum.

1, 2, 3, 4. Diagrams (1) showing normal heart; (2) embryonic heart; (3) mirror picture of normal heart; (4) heart in usual type of pure congenital dextrocardia; (5) from Graanboom's case of pure dextrocardia (mirror picture). Note that the apex is formed by the left (pulmonary blood) ventricle. (From Nagel's article on Pure Congenital Dextrocardia in the *Deutsches Archiv. f. klin. Med.*, xvi, p. 572.) (6) Grunmach's case of pure congenital dextrocardia; arrest of development, persistent embryonic stage. Note that the apex is formed by the right (caval blood) ventricle. (From his article in the *Berl. klin. Wchnschr.*, 1890, page 22.) The auricles are designated "caval" and "pulmonary" (according to the veins they receive), instead of right and left, in order to show the difference in situation in the mirror picture and in Graanboom's case, from that of the usual type of pure congenital dextrocardia (Grunmach's case).

differentiated from dextrocardia of simple arrest (type *a*) by the reversed entrance of the caval and pulmonary veins in the transposed auricles and descent of the aorta on the right, and by the characteristic features of the electrocardiogram during life (*vide infra*). In both Lubs' and Graa-boom's cases the ventricular septum was entire and there were only minor anomalies of the vessels at the base.

FIG. 54



a. Electrocardiogram from a case of congenital "dextro-versio-cordis," *i. e.*, simple displacement of the heart to the right. Here there is no reversal of leads, but Lead I especially deviates from the normal in Q and R.

b. Electrocardiogram from a case of congenital dextrocardia with transposed (mirror-picture) heart. Note that: Lead I, is completely reversed in that P, R, and T, normally directed upward in this lead, here point downward. Lead II, has changed places with Lead III. (From *Clinical Electrocardiography*, Sir Thomas Lewis, London, 3d ed., 1924, p. 112.)

True or mirror-picture dextrocardia, unless associated with other anomalies, is not itself of clinical significance and may be discovered accidentally, with the heterotaxy that usually accompanies it, in a perfectly healthy subject, by physical and roentgen-ray examination, which reveals the normal area of cardiac dulness on the right side, with corresponding location of sounds and fluoroscopic findings. Such true or mirror-picture dextrocardia, of the type usually associated with situs inversus viscerum (Graa-boom's case) yields a characteristic electrocardiogram (Neuhof,¹ Lewis²), in that Lead I, shows an inversion of all curves and Leads II and III, replace each other. This supplies a diagnostic point between the transposed and non-transposed forms of congenital dextrocardia and also distinguishes the former from a dextroversion

¹ *Jour. Am. Med. Assn.*, 1913, 60, p. 1064.

² *Clinical Electrocardiography*, 1924, p. 115.

in which the electrocardiogram, although atypical, is not reversed. Jones¹ classes the three types as (1) mirror picture dextrocardia; (2) dextroversion (*a*) acquired during fetal life and (*b*) acquired after birth (dextroversion proper). We prefer Nagel's nomenclature because in dextrocardia due to arrest or "fetal dextroversion," the heart is not pulled or pushed over to the right but remains there as a result of interference with the normal processes of growth.

Incomplete Heterotaxy.—Of interest are four cases reported by Hickman,² Griffith,³ Royer and Wilson⁴ and one in the McGill Museum, reported by the late Dr. John McCrae of transposition of the viscera with only partial transposition of the heart, which maintained its normal position with *apex pointing to the left*, the ventricle and auriculo-ventricular ostia unchanged, but the auricles and great arterial trunks transposed, and the auricular septum defective. In McCrae's and Hickman's cases the pulmonary artery was atresic, in those by Crozier Griffith and Royer and Wilson it was stenosed, and arose from the right ventricle with the aorta but in transposed relation. The ventricular septum was entire in McCrae's case, defective in the other two. In the remarkable and still more *bizarre* case of Keith and MacDonnell⁵ a complete situs inversus of the viscera with dextrocardia, the heart lay on the right of the median line with *apex pointing to the right* and transposed auricles, but the ventricles, auriculo-ventricular valves and stems of the great trunks were not transposed, yet at their origin the aorta and pulmonary artery had themselves undergone transposition or reversed torsion, so that the aorta arose from the right (tricuspid), and the pulmonary from the left (mitral) ventricle; no veins however entered the auricle on the right side, but both cavæ and pulmonary veins emptied into a common sinus venosus on the left and passed thence into the left auricle and through the left ventricle into the much dilated pulmonary artery, which supplied the systemic circulation through a small patent ductus. The infant presented moderate cyanosis but no clubbing and no murmur, and died of bronchopneumonia.

Intrinsic Displacement of Chambers.—Interesting examples, in anencephaly and ectopia cordis, of displacement of the chambers upon each other as a result of extraneous mechanical force exerted on the heart after it was fully formed, are reported by Jane Robertson,⁶ and recently by Holmes (*loc. cit.*, p. 660).

ANOMALIES OF THE HEART AS A WHOLE

Acardia, Hemicardia.—Where grave interference with the circulation occurs at a very early embryonic period, the heart may not develop at all (acardia), or it may be rudimentary (hemicardia). Such a condition usually develops in one member of a uniovular twin pregnancy in which

¹ *Brit. Med. Jour.*, 1924, i, 147.

² *Trans. Path. Soc.*, London, 1869, 20, 88.

³ *Univ. Med. Mag.*, Philadelphia, 1899.

⁴ *Arch. Pediat.*, 1908, 25, 882.

⁵ *Proc. Roy. Soc. Med., Sect. Med.*, 1921, 14, No. 3.

⁶ *Jour. Path. and Bact.*, 1913, 18, 211.

anastomosis of the vessels of the two individuals can take place through their common placenta.

All degrees of acardia may occur and from the developmental standpoint the findings are extremely interesting. Thus Campbell and Shepherd report a case in which the circulation had been interfered with before the heart had formed at all, and in which the two dorsal arteries passing from the umbilical opening toward the head of the amorphous monster, represented a persistence of the early vitelline circulation. Kehrer¹ adds to an analysis of thirteen cases from the literature an account of a case of his own which is remarkable for the advanced state of the rudimentary organ. Cases not included in Kehrer's review are reported by Schubert² and by Näcke and Benda.³

Multiple Hearts.—This phenomenon is commoner in animals. An explanation is perhaps to be sought in an irregular division of the omphalomesenteric or vitelline veins, from which the first heart *anlage* is derived.

Bifid Apex.—This may occur without other anomaly or complicating grave defects. The apex of the early embryonic heart during its amphibian stage, is bifid; a condition to be ascribed to the rapid downward growth of the apices of both ventricles at this time, so that a deep interventricular groove or cleft is formed. Obliteration of this cleft takes place in embryos over 11 mm. long, by the development downward of the embryonic apex, which occurs simultaneously with the closure of the interventricular foramen. In the adult mammalian heart bifid apex is thus to be ascribed to a persistence of the interventricular groove (Gegenbaur), due to an arrest of development of the embryonic apex, as is evidenced by the absence of the muscular vortex normally present here, each apex in the bifid state being formed independently from musculature derived respectively from the musculospiral and sinospiral bands (Mall).⁴ A deeply bifid apex is normal in the dugong; it occurs in 3 of Thérémis's 106 cases and in 15 of our series.

Diverticulum.—The heart may be prolonged into a hollow process. Arnold⁵ reports a female child, aged two and a half months, a subject of congenital lues, in whom the apex of the left ventricle ran out into a hollow process which bent around like a hook, its blind end projecting upward and to the left. In Koller-Aeby's⁶ case it formed a pulsating process with muscular walls descending from the apex of the left ventricle through a defect in the diaphragm to form part of an umbilical hernia. Diverticulum of the heart is rare and of no clinical significance.

Primary Congenital Hypertrophy.—In 1898, Simmonds⁷ reported the first clear case of primary congenital hypertrophy. In a newly born child which died during a protracted labor all the organs including the kidneys were normal, but the heart was greatly enlarged. It weighed 44 gm. (normal weight 19 to 20 gm.); the right ventricle was 0.75 to 1 cm., the left 1 to 1.25 cm. thick. The papillary muscles were small and took no

¹ *Arch. f. Gynäk.*, 1908, **85**, 121.

² *Zentralbl. f. Gynäk.*, 1907, p. 17.

³ *Virchow's Arch.*, 1894, **137**, 318.

⁴ *München. med. Wchnschr.*, 1898.

⁵ *Monatsch. f. Geburts.*, 1908, **28**, 3.

⁶ *Anat. Rec.*, 1912, **6**, 167.

⁷ *Arch. f. Gynäk.*, 1907, **82**, 185.

part in the hypertrophy. Other typical cases of congenital hypertrophy without valvular disease or nephritis, are reported by Effron,¹ Kalb,² Ratner,³ Hedinger and Howland,⁴ and Carrington and Krumbhaar.⁵ Dr. Howland (1919) made a full review of some 20 cases which he found in the literature, and added 5 personal observations in children ranging from ten months to four years in whom the diagnosis was made by him during life from great cardiac enlargement in the absence of adequate cause or characteristic murmurs, dyspnoea and weakness of sudden onset and unexplained origin, "fainting-spells," and cyanosis slight or absent or present only during the "attacks." Sudden death occurred in all his 5 cases and appears to be the usual termination.

The etiology is obscure, the theories advanced remaining hypothetical. In the recent case by Carrington and Krumbhaar⁸ (1924) in an infant, aged ten months, a second anomaly existed in that the left coronary arose from the pulmonary artery and the myocardium was diseased, showing a diffuse fibrosis, and parenchymatous degeneration of the region supplied by the anomalous coronary. This was not considered sufficient to account for the degree of hypertrophy that existed, but was regarded nevertheless a suggestive feature. A similar (unpublished) case has been communicated to us by Dr. J. A. Stevenson from the service of Prof. E. T. Bell. An infant aged three months presented marked pallor and slight cyanosis, and increasing hoarseness, apparently due to compression of the recurrent laryngeal nerve by the enlarged left auricle. Autopsy showed marked hypertrophy and dilatation of the left chambers with resultant compression of the left bronchus and atelectasis of the left lung, marked thinning of the left ventricle near the apex with scattered areas of myocardial fibrosis and anomalous origin of the left coronary from the pulmonary artery.

Congenital Rhabdomyoma.—An interesting problem is presented by the occurrence in infants or young children of embryonic muscle tumors of the heart wall associated, in the majority of the cases, with sclerosis of the cerebral cortex. The condition was first described by von Recklinghausen and by Virchow (1864) and was first reported on this continent by Knox and Schorer.⁶ Wohlbach⁷ studied the 11 cases on record, and added an observation of his own, in which a rhabdomyoma of the wall of the right ventricle was associated with multiple nests of neuroglia in the spinal meninges. The child, a female, with hydrocephalus and spina bifida and paralysis of the lower half of the body from birth, died of scorbutus at ten months. The heart was very large, weighing 72.5 gm., with hypertrophied papillary muscles. Just below the pulmonary valve an ovoid nodule, 1.7 x 4 cm. of grayish-red color and elastic consistence, lay imbedded in the interventricular septum and in the papillary muscle of the anterior tricuspid segment, to which it supplied chordæ. Microscopically it was composed of a delicate reticulum of connective tissue

¹ *Zurich Thesis*, 1903.

² *Munich Thesis*, 1906.

³ *Berlin, Thesis*, 1912.

⁴ *Contrib. Med. and Biol. Research, Osler Anniv. Vol.*, P. B. Hoeber, N. Y., 1919, 1, 582.

⁵ *Am. Jour. Dis. Child.*, 1924, 27, 447.

⁶ *Arch. Pediat.*, 1906, 23, 361.

⁷ *Jour. Med. Research*, 1907, 16, 495.

supporting heterogeneous cells having a more or less irregularly striated fibrillary matrix and containing in many instances large intracellular spaces and peripherally placed nuclei, the whole bearing a *bizarre* resemblance to the Purkinje fibres of the adult heart. Steinbiss¹ has recently (1923) presented a careful study of 30 cases, including 6 personal observations, the latter in subjects ranging from five to thirty-five years who were all under institutional care for idiocy or epilepsy the result of the cerebral sclerosis. In 3 of his cases the characteristic rhabdomyomatous nodules occurred scattered through the myocardium, in 1 as pedunculated polyps from the right auricular appendix, in 1 as pin-head transparent growths sprinkled over the endocardium of both ventricles, and in 1 in a mass of gelatinous subepicardial fat. He concluded that: (1) the condition is not limited to early childhood; (2) the cardiac growths are practically always associated with disseminated nodules of embryonic tissue in the brain and renal cortex and frequently also with a papillomatous condition of the skin; (3) these lesions are of the nature of an excess formation, the result of a general metabolic disturbance occurring at a very early stage; (4) the cells, while retaining their embryonic type, become highly differentiated structures which are predisposed to early retrogressive changes (vacuolation, calcification), and a replacement fibrosis takes place, precluding malignancy, which does not occur. Uehlinger² (1925) has brought the number of recorded cases to 39, of which 30 are multiple, 7 are solitary and 2 (those by Schmincke and himself) are diffuse.

A remarkable (unpublished) case of massive rhabdomyoma of the right ventricle occluding the tricuspid orifice occurred in a female patient aged seventy-four years, from the service of Dr. C. P. Howard at the Montreal General Hospital, who died after an illness of some three weeks. At autopsy a large tumor 6 x 4.5 cm. was found in the musculature of the right ventricle partly involving the septum and passing down to the apex and with a clublike extension 2 cm. long projecting through the tricuspid ring into the right auricle. Histologically it was a typical rhabdomyosarcoma, composed of large irregularly shaped multinucleated cells and of large spindle cells forming an intercellular substance resembling smooth muscle and presenting a cross striation in some places, and metastases had extended into the mediastinal lymph nodes, lung and pericardium.

Congenital Heart-block.—This is rare but of great interest from the physiological standpoint and from that of the cardiac anomaly which is nearly always associated. Of the cases reported, only those which have been proved by graphic records to show a true dissociation, and in which the history of the block dates back to early childhood as pointing to a congenital origin, are included in the valuable statistical reviews recently published. Of such cases there appear to be 16 in the literature. Carter and Howland³ (1920), in the first comprehensive study made, collected 7 such cases published up to that time, and added 1 of their own in a girl, aged ten years, with a ventricular rate of 44, diagnosed as complete heart-block by electrocardiograph at eight years, and who presented a harsh systolic murmur over the precordium with maximum intensity at the

¹ *Virchow's Arch.*, 1923, **213**, 22.

² *Arch. f. klin. Med.*, 1925, **258**, 719.

³ *Johns Hopkins Hosp. Bull.*, vol. **31**, 351.

third left interspace. In 4 of the 8 cases a complete block was demonstrated: that by Van der Heuval (1908) was in a woman aged twenty-three years, with a history of severe syncopal attacks from infancy, a harsh systolic murmur with maximum intensity at the third left interspace and a ventricular rate of 34; that by Fulton, Judson and Norris (1910) in a child aged twenty-two months, with ventricular rate noted on the seventh day of 42 per minute, and a loud systolic murmur over the precordium; that by d'Espine of a boy aged eight years, with a history of a single syncopal attack, and an auricular rate of 104 as against a ventricular beat of 26; and that by Rorenson of a girl aged ten years, who came under observation at eight years with ventricular beat of 44 and a loud sawing diastolic murmur with maximum intensity at the second left interspace, thought to be due to a communication between the base of the aorta and pulmonary artery. In the other 3 cases cited the block was partial, in 2 (Wipham and Bass) alternating with complete dissociation, and in the third case (Wipham) a simple 2-1 block. A noteworthy feature in these cases was the absence, except in Van der Heuval's case, of serious syncopal attacks, a feature that Howland thought might indicate their congenital origin, as evidencing an early adaptation of the conducting mechanism of the altered path of the *A-V* fibres. In all of these cases but one cyanosis was absent, and the clinical picture was that of a cardiac septal defect.

White, Eustis and Kerr¹ (1921), added 3 cases, those reported by Görter, and Lewis, and a unique personal observation of an infant in which the arrhythmia was discovered in the fetal heart-sounds eight hours before birth, and the electrocardiographic proof of a partial 2-1 and 3-1 block was established on the fourth day of life. There were no murmurs, but cyanosis was present on crying, and the child was a typical Mongolian idiot. The frequent combination of the latter condition with cardiac septal defects is well known, and its occurrence in many cases of persistent ostium primum has already been noted. In this connection its association here with evidence of a cardiac anomaly and disturbed conductivity is of great interest in the light of the histological investigation made by Morison² (1912) into an anomaly of this type (foramen primum). Careful serial sections made by him in the region normally occupied by the central fibrous body and *A-V* bundle at the foot of the defective auricular septum showed the node displaced posteriorly and below the coronary sinus, and an anomalous course of the fibres, in that these split in emerging from the node into an abortive left branch which coursed in the left auriculo-ventricular groove but failed to reach the left ventricle, and a larger right branch which divided lower in its course to supply the left as well as the right ventricle. Such a distribution might explain minor disturbances of conductivity evidenced by changes in the ventricular complex as seen in a case by E. Baumgartner (cited below.)

Romberg and White³ (1924) assembled 3 more cases, 2 reported by Frias, and by Barbier, Lebée and Mouquin, and a personal observation of their

¹ *Am. Jour. Dis. Child.*, 1921, **22**, 299.

² *Proc. Royal Soc. Med.*, 1912-1913, **6**, Pt. 1.

³ *Boston Med. and Surg. Jour.*, 1924, **190**, 591.

own in a child, aged ten months with an auricular rate of 160 and ventricular of 70. In addition there is a case by Nobécourt¹ (1924) of an infant aged ten months with cyanosis and polycythemia. In none of these 15 cases of proved congenital heart-block was an autopsy obtained nor the course of the *A-V* bundle studied. This has been done by Wilson and Grant⁵ who published the first case of proved heart-block with autopsy findings and a complete histological study of the bundle region. In a child, aged fourteen months, presenting a partial (2-1 and 3-1) heart-block with marked cyanosis, clubbing, and polycythemia, the autopsy showed a pulmonary atresia in a trilobulate heart and the interventricular septum completely absent except for a low muscular prominence at the back of the common ventricle which represented its posterior limb. Microscopic examination of tissue at the junctional area, showed the *A-I* node in its normal position but the main trunk of the bundle lay upon the upper part of the muscular prominence representing the defective septum just beneath the thickened endocardium and, descending on this to be distributed to the left part of the ventricle, gave off a large right branch which showed beneath the endocardium on the right side of the prominence as a faint whitish ridge and which supplied the right side of the common chamber. The fibres which followed this anomalous course were nowhere degenerated, but changes were found in the auricular part of the bundle before its division.

The importance of this contribution can scarcely be overestimated. That the *A-V* fibres and node are liable to deflection in cardiac anomalies involving the path normally occupied by these structures had been clearly shown by Monckeberg² in his topographical studies, and by others; but that such deflections are actually the cause of abnormalities of conduction is first demonstrated by Wilson and Grant. The assertion is now justified that the cause of congenital heart-block lies in the great majority of cases in the deflection or interruption of the *A-I* bundle in some part of its course through the mechanical conditions imposed by the associated cardiac anomaly. In a few cases, of course, gross lesions of the myocardium invading the main trunk of the bundle, the result of congenital syphilis (von Zalka), or of extension from a mural endocarditis (Starck³), may produce a congenital dissociation just as is the case in the adult heart.

Minor alterations in conductivity due to an abnormal distribution of the propagated impulse may occur as in a case about to be reported by E. Baumgartner and might be explained by a low branching of the bundle such as took place in Morison's case.

ANOMALOUS BANDS AND SEPTA

Anomalous cords, bands, or septa may arise within the heart, and lead, when sufficiently pronounced, to a division of the chambers, and the so-called double or supernumerary cavities.

Anomalous Septa in the Left Auricle (Double Left Auricle).—Of this interesting condition there are 10 fully reported cases, by Church

¹ *Heart*, 1925-1926, **12**, 295.

² *Atlas der Missbildungen*, Jena, 1912.

³ *Monatsch. f. Kinderheilk.*, 1903, **2**, 11.

(1868), Fowler, Martin, Griffith (2 cases), Potter and Ransom, Borst, Hosch,¹ Stoeber, and William and Abrikosoff,² the first eight of which are summarized in Hosch's article. In these cases, a membranous diaphragm perforated by one or more openings stretches across the left auricle, dividing it into a right postero-superior chamber, which receives the pulmonary veins and contains the interauricular septum, and a left antero-inferior chamber, in which lies the auricular appendix and the mitral orifice. The blood from the pulmonary veins enters the large upper chamber and passes thence through the small opening in the diaphragm into the lower chamber to the mitral orifice. When the foramen ovale is patent, a large portion of the pulmonary blood may pass through the open foramen into the right auricle, thus depleting the greater circulation and throwing the bulk of the work on the right heart, which, as in this case, becomes greatly hypertrophied, and the left chambers very small.

Borst gives a careful anatomical study of his case, which throws much light on the etiology. In a woman, aged thirty-eight years, dying with failing compensation, the right ventricle was much hypertrophied and dilated, and the left auricle was greatly dilated. There was no communication between the auricles, but the *valvula foraminis ovalis* was absent. The left auricle was divided into a large upper cavity receiving the pulmonary veins and a small lower chamber containing the mitral orifice by a diaphragm which ran from above anteriorly and externally, downward, inward and backward. This diaphragm presented at its insertion below and behind, a round hole, 1 cm. across, which was the only communication through which the blood from the pulmonary veins could be transmitted to the mitral orifice.

Borst explained this anomalous diaphragm as the malposed *septum primum* which had been deflected to the left in the embryonic heart by a displacement of a pulmonary vein to the right, so that it entered the auricles between the *septum primum* and *secundum*, and had thus formed between them this large secondary cavity. The hole in this anomalous septum, which communicated with the smaller cavity below, he looks upon as the *ostium secundum* (foramen ovale). This theory was supported by William and Abrikosoff,³ who made a histological study of the anomalous septum and found it to be the same as and directly continuous with the wall of the left auricle behind and to the right, while anteriorly and to the left, where it evidently became attached in later embryonic life, it was quite different. In their case the edges of the small opening in it were fringed with vegetations.

Borst's explanation receives further striking corroboration from what may be termed a complementary case reported by Sternberg,⁴ in which three auricular chambers were present, separated from each other by strong septa. The left chamber received the pulmonary veins and contained the mitral orifice, and communicated with the middle chamber by a large ovoid foramen (the *ostium primum* of Born), situated in the

¹ *Frankf. Zeitschr. f. Path.*, 1907, **1**, 56.

² *Virchow's Arch.*, 1911, **203**, 404.

³ *Virchow's Arch.*, 1911, **203**, 404.

⁴ *Verh. der XVI Deut. path. Gesell.*, 1913, p. 256.

lower portion of the anomalous septum (*S. primum*) just above the mitral valve. This middle chamber received the superior cava only and communicated with the remainder of the right auricle, which received the inferior cava, by a large opening. Sternberg explained the formation of the middle chamber by a displacement to the *right* of the septum secundum, due to a malposition of the inferior cava, which entered too far to the *left*, and pushed the septum secundum to the *right*, just as in Borst's case the anomaly was due to the entrance of the pulmonary veins too far to the *right*, so that they cut off a middle chamber by pushing the septum primum to the *left*.

Anomalous Septa and Networks in the Right Auricle.—These are quite different both in structure and origin from those in the left auricle. The condition was first described and figured by Chiari¹ on the basis of 11 original cases. In all these a system of fine cords, or a reticulum of delicate tissue identical in structure with the Eustachian valve and attached to this or to the Thebesian valve, stretched across the auricle to be attached to the crista terminalis or auricular septum or other points, and are to be ascribed to a persistence and anomalous development of the *septum spurium* or of the right or left *valvula venosæ*. These are the lips of the opening of the embryonic sinus venosus into the right auricle. In the normal development they become merged with the Eustachian and Thebesian valves, and with the septum secundum. In a case by Lesieur and Froment² of a gaping foramen ovale with an anomalous valve of Thebesius, 6 cm. high, which projected as a fenestrated, incompletely attached, shelf across the right auricle, these authors ascribe both anomalies to the maldevelopment of the *valvula venosa sinistra*, which failed to close in the foramen ovale by merging with the septum secundum. A connection between these two anomalies is further established in Ebbinghaus's case, in which Chiari's fenestrated network extended across the auricle from the Eustachian valve, and the interauricular septum showed fifteen small and two large perforations. Persistent left superior cava is also frequently associated.

Clinical Aspects. When uncomplicated by other defects, such septa may exist without giving any evidence of their presence. All the cases of double left auricle recorded were in adults, except that by Hosch. There are certain dangers, however. When the septum is strongly developed, it is liable to hamper the blood stream. Church's case, and Borst's, both died at thirty-nine years of failing compensation, and Borst's patient suffered from earliest youth from dyspnoea, while in the case of "double left auricle" reported by William and Abrikosoff, in an underdeveloped boy aged eleven years, dying with marked anasarca, the lungs were the seat of extreme passive congestion and the smaller branches of the pulmonary veins were thrombosed, a condition significant of the back pressure that existed in the upper left chamber. Again, the fine reticulum that occurs in the right auricle may supply a possible nidus for thrombotic processes, which may lead to pulmonary embolism and death.

Anomalous Septa in the Ventricles.—These again have a very different origin from those in the auricles. The commonest form is a septum

¹ Ziegler's *Beitr.*, 1897, 22, 1.

² *Lyon Méd.*, 1911, 96, 1045.

shutting off the conus from the sinus of the right ventricle, which probably represents arrest at an early stage in the development of the heart, explained by Keith as a "persistence of the lower bulbar orifice." Such septa have usually undergone much fibrous thickening, and have been ascribed by many observers to inflammatory contraction, but in a case reported by Bohm all evidence of fibrosis was absent, and the conus was separated from the sinus by a simple muscular ridge. Two cases reported by Stephen Mackenzie¹ of hearts showing "three ventricles," separated by incomplete septa, probably belong here. So also in the case of an accessory or "fourth ventricle" reported by Dudzus,² in which the dilated and dextroposed aorta arose to the right of a defect in the interventricular septum entirely from the right ventricle, and a small pulmonary artery with bicuspid valve sprang from a miniature cavity occupying the position of the conus (fourth ventricle), which communicated with the "third ventricle" or cavity at the root of the dextroposed aorta by a very narrow orifice.

In another type of anomalous septum, a rudimentary chamber giving off the pulmonary artery or the (transposed) aorta is cut off from a common ventricle which receives both auriculo-ventricular orifices, by what appears to be the malposed and defective interventricular septum. This type is well illustrated by the Holmes specimen in the McGill Museum (described and figured under triloculate heart, page 702). There are 9 similar cases in the literature including that by E. S. Mills,³ but in all except that of Holmes the aorta and pulmonary artery were transposed.

Anomalous chordæ tendineæ frequently cross the ventricles at irregular points. They may consist of fibrous tissue with or without ordinary heart muscle fibres, or they may contain fibres from the auriculo-ventricular bundle. These fibres have been studied by Tawara,⁴ who gives a review of the literature, and by Mönckeberg.⁵ Three classes may be distinguished (H. T. Lewis⁶): (a) Those passing along the walls of the ventricles: these are of no clinical significance. (b) Those passing from auricle to ventricle. (c) Those stretching across the cavity of the ventricle. It is in cases of this latter type that loud musical murmurs are produced, varying in rhythm according to the site of attachment of the anomalous cord and the moment in the cardiac cycle when the string is rendered taut. This is usually in systole, as in 2 cases by Wayne and Huchard.⁷ It may however be diastolic. A case in point is related by Hamilton.⁸ The patient was a man of forty with symptoms of aortic insufficiency, who presented, in addition to a soft diastolic murmur with the localization characteristic of this lesion, a second murmur, also diastolic, but musical in character, which had its maximum intensity at the third left interspace, but was widely propagated over the chest, and was so loud as to be audible 2 feet away from the patient. The autopsy, performed

¹ *Trans. Path. Soc.*, London, 1880, **31**, 63.

² *Jour. Med. Research*, 1923, **44**, 257.

³ *Verhand. XII Deut. Path. Gesell.*, 1908, p. 160.

⁴ *Trans. Chic. Path. Soc.*, 1897-99, **3**, 145.

⁵ *Montreal Med. Jour.*, 1899, **28**, 508.

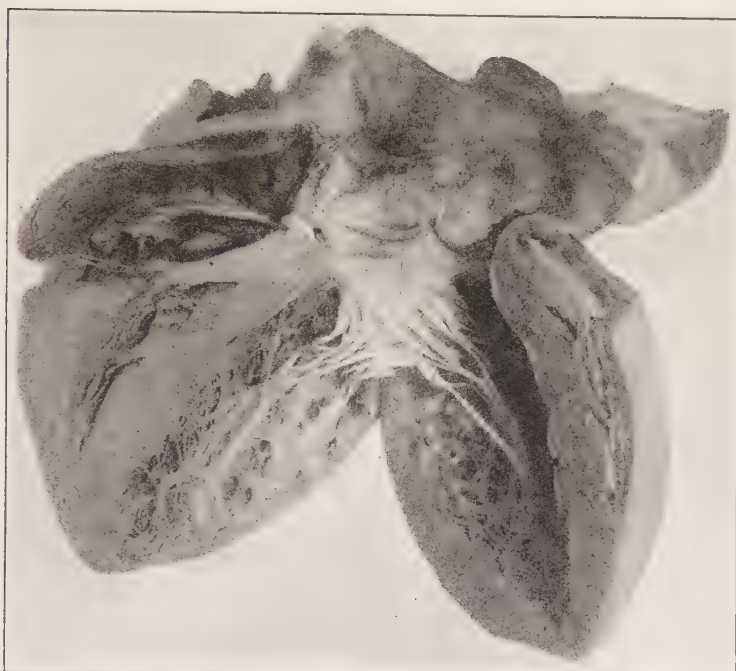
⁶ *Arch. f. klin. Med.*, 1923, **243**, 24.

⁷ *Ziegler's Beiträge*, 1906, **39**, 563.

⁸ *Revue de Med.*, 1923, **13**, 13.

by Adami, showed this musical murmur to have been produced by an anomalous cord which sprang from a small papillary muscle of its own, and crossed the auricular surface of the aortic cusp. The aortic valves were thickened and incompetent. (See Fig. 55.)

FIG. 55



Aberrant chordæ tendinæ in left ventricle producing a loud musical murmur. (From a specimen in the McGill Medical Museum, presented by W. F. Hamilton and J. G. Adami. Reported by W. F. Hamilton.)

Anomalous Chordæ Passing from Auricle to Ventricle.—These are rare and of great embryological interest, although probably of little clinical significance. De Vecchi¹ describes and figures, in the heart of a man, aged sixty-nine years, a cord 3 cm. long “shaped like a needle” which ran from the lower border of the valvula foraminis ovalis on the left side of the auricular septum down to its attachment in the free border of the aortic segment of the mitral valve; the foramen ovale showed a slight valvular patency. He refers to 3 other such cases in the literature and believes this tendinous cord to be a remnant of “some modification of the intermediary septum and left endocardial pad, which has extended downward following the mitral valve in its development and upward following the development of the interauricular septum, to the superior limit of this, *i. e.*, to the limbus of the foramen ovale.” This account is of great interest in explaining the extraordinary case recently reported by Goforth,² of a smooth glistening rounded thread-like cord arising from

¹ *Anat. Anzeiger*, 1901, **20**, 374.

² *Jour. Am. Med. Assn.*, 1926, **86**, 612.

the right auricular wall 1.5 cm. from the annulus ovalis which ran unattached toward the slightly patent foramen and apparently obliquely pierced the auricular septum just below this and emerged in the left auricle where it was attached to the lower part of the auricular septum at the same point as was the cord in de Vecchi's case, and, following the course of the blood flow, passed downward through the mitral orifices well into the left ventricle where it turned and, "assuming a parabola curve" around the anterior mitral leaflet, proceeded upward to the aortic segment which it pierced perpendicularly and became attached to the wall of the aorta 8 mm. beyond. It was thickest in its middle portion where it curved round the mitral leaflet. Microscopically it contained no muscle of any variety but wavy collagenous fibres with scanty endothelial covering, evidencing that it did not originate from the primitive muscle of the ventricle as in the chordæ which cross this.

In 3 cases described by Rolleston, Griffith, and Brociewicz,¹ an anomalous cord rose from a rudimentary papillary muscle in the left ventricle and passed upward into the auricle to be attached to the lower part of the auricular septum at exactly the same point.

Anomalous Bands in the Arterial Trunks.—Anomalous chordæ passing from the aortic cusps to the base of the aorta (Rohrle), and from pulmonary cusp to base of pulmonary artery (Poscharissky) have been recorded. An anomalous band within the aorta crossing its lumen from a point of attachment above on the convexity of the arch to one on its concavity below, is reported by Lucksh, and by Christeller.² In the latter's case, a man, aged twenty-nine years, a thread-like cylindrical flattened body identical in its histological structure with the wall of the aorta and with smooth intimal covering passed perpendicularly downward with a slight convex curve to the back from a point near the innominate orifice, incompletely dividing the lumen of the aorta into two parts. Both authors believe that it represents a persistence of the wall dividing the right and left (fourth) embryonic aortic arches.

DEFECTS OF THE INTERAURICULAR SEPTUM

These may consist of a simple patency of the foramen ovale, or true defects of the interauricular septum, situated above or below the foramen, and single or multiple, may occur. In this series, the foramen ovale was patent 258 times, and there were 54 true interauricular septal defects uncomplicated by other anomalies, of which 16 were in its upper and 24 in its lower part, and 13 were multiple. In 9 cases the septum was rudimentary and in 9 it was absent (cor biventriculoculare).

Patent Foramen Ovale.—This orifice, which in the fetus is widely open, allowing of the passage into the systemic circulation of aërated placental blood, usually closes after birth, but its persistence in adult life as a valvular slit is so common that this can scarcely be considered abnormal. Among 711 adults, Zahn found the foramen open in 139, and in Adami's records of 1374 autopsies at the Royal Victoria Hospital,

¹ *Virchow's Arch.*, 1896, **145**, 649.

² *Beitr. z. path. anat. Zieg.*, 1924, **32**, 173.

Montreal, it occurred 199 times (14.5 per cent.). From the combined statistics of Bizot, Ogle, Klob, Wallman, Rostan and Hinze, we learn that among 2087 hearts examined, the foramen was patent 632 times (30 per cent.) (Herxheimer).

A widely patent foramen is, however, a true anomaly, which, by allowing free communication between the auricles, may give rise to various disturbances. Of the 258 cases in this series, 112 were of this type, and of these, 32 were instances of pure patency, unassociated with other defect, and were therefore classed as the primary lesion, as affording material for the study of special symptoms and signs. In some cases the opening is very large, the size of a "two-shilling piece" (Peacock), in others it is a "circular opening with thickened edges admitting a penhandle," and in others again, it is valvular in form but an elliptical gap remains between the concave free margins of the annulus ovalis and the valvula foraminis ovalis, which are here incomplete.

The causes of patency may lie in a rise of pressure in the right chamber after birth, preventing the firm apposition of the valvula foraminis ovalis from the side of the left auricle, and its subsequent closure; this is the case in the majority of the cases complicating other defects, such as pulmonary stenosis. Or the foramen may remain open as a result of a true arrest of growth of the primitive septa, especially of the septum secundum, an event which may be shown in the specimen by an incomplete development, absence, or fenestration of the annulus ovalis. The association of an anomalous network springing from the Thebesian or Eustachian valve, with a patent foramen or perforated valvula foraminis ovalis, and the dependence of both anomalies on the persistence of the embryonic sinu-valvular apparatus, has been mentioned. Persistence of the left superior vena cava belongs to the same complex, as is illustrated by its occurrence in the case of Berthel.

Defects in the Upper and Posterior Part of the Interauricular Septum.

—These are extremely rare. Two types may be distinguished, one in which the defect is associated with an anomalous disposition of the great veins, which is probably the primary condition, and another in which no such associated anomaly has been demonstrated, and which on closer investigation may be found to belong in the same category with the first, or which may require a different explanation. A series of cases has been recorded, in which a large defect occupies the upper margin of the auricular septum, directly under the orifice of the superior vena cava, which is displaced somewhat to the right, so that its orifice looks into both auricles through the defect. A displacement to the right of the pulmonary veins, so that these enter either the superior vena cava just before this vessel reaches the heart, or the right auricle itself, has been noted and is to be considered the primary anomaly. Paltauf thought that the hole in the septum was not a defect at all, but represented the orifice of the right pulmonary vein, which entered here directly above the septum, with the superior cava. In Hepburn's case the wall of the auricles was directly continuous with the wall of these two veins, which here entered the auricle together. The foramen ovale was patent in some cases, and is mentioned as closed in others.

Rokitansky described 7 cases of a similar anomaly, in which the *inferior cava* looked into both auricles through the defect. In one of these the right pulmonary veins entered the right auricle.

In a specimen in the McGill Museum, reported by Abbott and Kaufmann¹ (see Fig. 56), a large ovoid defect 3 x 3.5 cm. in diameter occupies the upper and back part of the septum, but the superior cava is not displaced, but enters the right auricle in its normal situation and is separated from the defect by a strong muscular cushion. The position

FIG. 56



Defect in the upper part of interauricular septum (persistent ostium secundum), with pulmonary dilatation, sclerosing pulmonary endocarditis with calcification and hypoplasia of the aorta. From a woman, aged sixty-four years, dying of failing compensation with marked terminal cyanosis setting in during the last six months of life. Right chambers laid open to show: A, hypertrophied and dilated right auricle; B, large defect in the upper part of interauricular septum bounded below by C, a stout muscular partition, the defective auricular septum; D, absence of annulus ovalis and of Eustachian valve; E, dilated coronary sinus guarded by a defective valve of Thebesius; F, entrance of superior vena cava; G, entrance of inferior vena cava. (From a specimen in the Medical Museum of McGill University, Montreal. Presented by F. W. C. Mohr. Reported by M. E. Abbott and J. Kaufmann.)

of the right pulmonary veins could not be ascertained, but the annulus ovalis and Eustachian valve are absent, and it is probable that we are here dealing with an entirely different condition, namely, a huge persistent ostium secundum (patent foramen ovale) which has escaped closure through lack of development of the secondary septum. The heart was from a woman of sixty-four in good health until the last six years

¹ *Jour. Path. and Bacteriol.*, 1910, **14**, 525.

of life, when cyanosis began to manifest itself. The case terminated with failing compensation and profound cyanosis, and is further remarkable in that extensive endarteritic changes with extreme calcification had taken place in the pulmonary valves, as the result of the excess of work done by the pulmonary circulation.

Defects in the Lower Part of the Interauricular Septum.—These are somewhat more frequent than are defects at the upper part of the septum, but are also rare. They are explained as a persistence of the *ostium primum*, the septum primum having failed to descend and unite with the cushion between the auriculoventricular orifice. Such a defect has a very characteristic appearance. It lies directly above the ventricles, may be of very large size, and is of a crescentic or semilunar shape, the thin border of the auricular septum, which forms its upper boundary, arching across the venous ostia to join the lower margin formed by the bases of the mitral and tricuspid valves, which are commonly deformed.

A common and interesting associated anomaly is a division of the anterior segment of the mitral valve, which is cleft from its free border up to its insertion, the two parts converging here to an acute angle, being widely separated below. In 5 of the 7 cases of this defect reported by Rokitsansky this cleavage occurred. It is well seen in Fig. 57, from a specimen in the McGill Museum. Here the foramen ovale was closed, as in the cases reported by Griffith,¹ Söldner,² Moore,³ and Peacock.⁴ It was patent in the cases by Reineboth,⁵ Thomson,⁶ Kilduffe,⁷ Sternberg,⁸ and in a case in the McGill Museum shown on page 759 (Fig. 88), in which the mitral segments formed a continuous ring, cleft anteriorly, in the left posterior portion of which lay a double mitral orifice with perfectly formed papillary muscles and chordæ tendinæ of its own.

Multiple Defects.—The valvula foraminis ovalis is not infrequently perforated by numerous small openings, as in a specimen (Fig. 58) in the McGill Museum, and in several cases in this series. This recalls the fenestrated septum seen in birds, and suggests an arrest of development at this stage. In a case reported by Dublitzhaja, of combined defects of the auricular and ventricular septa, the auricular septum, defective below, "hung like a curtain over the common ventricle," there was a large patent foramen ovale, and also a large hole at the upper and posterior border of the valvula foraminis ovalis. An almost identical case is reported by Ebbinghaus. In a man of fifty-two, there were fifteen small perforations and two large holes at either border, representing the persistent ostium primum and secundum (patent foramen ovale), and the right auricle contained an anomalous network.

Premature Closure of the Foramen Ovale.—Two cases have been reported under this title, one by Smith⁹ in an infant, aged twenty-one days, and the other by Sir William Osler,¹⁰ in a fetus still-born at the eighth

¹ *Med. Chron.*, Manchester, 1902, **4**, 383.

² *Trans. Path. Soc.*, London, 1881, **32**, 37.

³ *Deutsches med. Wchnschr.*, 1895, **21**, 870.

⁴ *Am. Jour. Med. Sci.*, 1914, **147**, 880.

⁵ *Trans. Path. Soc.*, London, 1846–1847, **1**, 57.

¹⁰ *Mont. Gen. Hosp. Repts.*, 1880, **1**, 77.

² *Munich Thesis*, 1904.

⁴ *Ibid.*, 1847, **1**, 61.

⁶ *Proc. Anat. Soc.*, 1902–3, vol. **36**.

⁸ *XVI Verh. d. Deut. Gesell.*, 1913, p. 253.

month with extreme anasarca. In both cases the fossa ovalis (*septum primum*) was very large, and bulged into the left auricle in an aneurismal pouch-like fashion indicating a greatly raised pressure in the right auricle before death. The specimen from Osler's case is in the McGill Museum (Fig. 59). In both cases the pulmonary artery was greatly dilated and supplied the descending aorta through a widely dilated ductus arteriosus and the aorta and left ventricle were small. In the case of the child living twenty-one days, there was marked cyanosis from birth.

FIG. 57

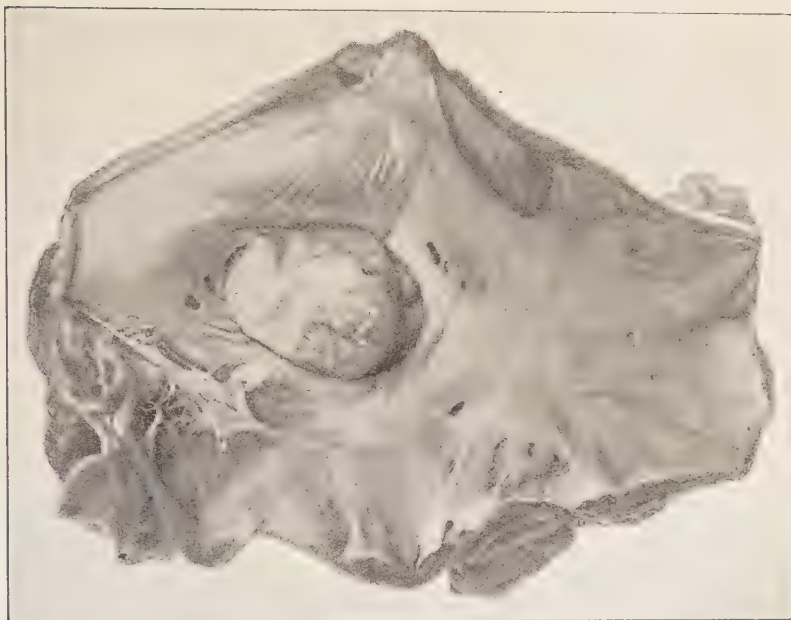


Heart showing (A) defect of interauricular septum below (persistent ostium primum), with (B) cleavage of right anterior segment of mitral valve. (C) Interauricular septum above showing closed foramen ovale. (D) Left posterior mitral segment. From a woman, aged thirty-two years, without cardiac symptoms, dying of perforative appendicitis. (Pathological Museum, McGill University.)

Aneurismal pouching of the fossa ovalis into the left auricle indicating raised pressure in the right auricle may occur, without any cardiac anomaly, as in a case reported by Peacock, and in Adami's case of multiple fenestrations (Fig. 58).

Secondary Pathological Changes.—The alterations in the circulation produced by large defects in the interauricular septum induce certain

FIG. 58



Fenestrated membrane bulging into fossa ovalis. (Pathological Museum, McGill University, presented by Dr. J. G. Adami.)

FIG. 59



Bulging of fossa ovalis into left auricle. Valvular patent foramen ovale. (From a specimen in the McGill Pathological Museum, presented by Dr. Osler.)

secondary results. Hypoplasia of the aorta and a corresponding dilatation of the pulmonary artery are almost always present, and the latter vessel may also be atheromatous from excessive strain. Hypertrophy and dilatation of the heart are the rule, and this may be confined to the right chambers which may be enormously enlarged, or it may be generalized, the changes in the right side almost always preponderating. In none of the cases in this series was the left ventricle hypertrophied in excess of the right. Congestive changes and œdema of the lungs, enlargement of the liver, and passive congestion of all organs usually occur as late results of the overloading of the pulmonary circulation.

Symptoms and Signs.—Large defects in the interauricular septum may exist without giving any sign or symptom and without interfering with the duration of life of the individual. The characteristic features of the majority of the cases may be summed up as an absence or but very slight manifestation of cyanosis except as a terminal phenomenon, in the presence of distinctive physical signs of the defect, and the clinical picture of hypoplasia of the aorta. This is particularly true of defects of the extreme *upper* part of the septum. Thus of 9 patients, 7 died of independent conditions. The 2 others died in advanced middle life from failing compensation apparently induced by the overloading of the pulmonary circulation and right heart in the arterial venous shunt that had undoubtedly occurred. In Greenfield's¹ case, a man aged fifty-three years, a hole $1\frac{1}{2}$ inches across lay directly beneath the roof of the auricle, and in that reported by Abbott and Kaufmann (Fig. 56), in a hardworking charwoman, aged sixty-four years, a huge defect 3 x 3.5 cm. occupied the same situation.

As pointed out by Bard et Curtillet such symptoms not infrequently develop in dramatic fashion after some intercurrent event such as a bronchopneumonia has caused a sudden rise of pressure in the right auricle with a resulting venous shunt into the left auricle and this may happen, not only in large gaping communications such as are described above and in persistent ostium primum, but also by the forcing open of a simple valvular patency, heretofore closed, as happened in their case in a man aged fifty-four years with a valvular patent foramen which at death admitted a pen-handle.

Pallor of the surface is a common characteristic (Mouls²) as is also a certain delicacy of build, the result evidently of the diminished amount of blood in the systemic circulation. Dyspnœa and tachycardia, bronchitis and signs of congestive changes in the lungs and of passive congestion in the viscera and enlargement of the liver are also common, from excess of blood entering the right heart. When, in adults with these symptoms, and with cyanosis slight, absent, or of extremely late appearance, we find distinctive physical signs of a defect localized over the upper and middle thirds of the heart, we may feel fairly sure that we are dealing with an auricular septal defect. In a woman, aged twenty-eight years, of somewhat infantile appearance, in whom cyanosis was entirely absent, a loud harsh systolic murmur with maximum intensity

¹ *Jour. Anat. and Phys.*, vol. 24, p. 423.

² *Rev. Mens. des Mal. des Enfants*, 1888, 6, 151.

at the third left interspace, 4.5 cm. from the midsternum, was heard all over the front of the chest and over the left back, the cardiac dullness was greatly increased in all directions, and there was a marked systolic thrill at the base to the left of the midsternum, extending downward to the top of the fourth rib. The neck veins were much distended, but no positive venous pulse was detected. Death occurred with symptoms of a chronic nephritis produced by what was pronounced by Adami to be congenital aplasia of the kidneys. The autopsy showed a large patent foramen ovale admitting the thumb, with cribriform perforation of the valvula foraminis ovalis, hypoplasia and slight coarctation of the aorta and infantile genitalia.

The freedom in the great majority of these patients from any evidence of cyanosis except as a terminal phenomenon, is well shown in the analysis of the 60 cases of auricular septal defects classified as the primary lesion in this series. Cyanosis was stated to be *entirely absent* throughout life in 12 cases, and in 14 others no mention was made of it and it was probably absent in the majority of these. *Terminal cyanosis* as a result of pulmonary complications or failing compensation was present in 24 cases and set in usually in the characteristic dramatic fashion. In 5 other cases cyanosis was mentioned as "slight," and of the entire series only that by Johnson¹ in an adult and 3 others in infants (Mackey, Simmons and Foster) showed it well marked. *Clubbing* of the fingers and toes was present also in Johnson's patient who died of failing compensation at twenty-seven years with a history of cyanosis from birth and of repeated hemoptysis. The heart presented extraordinary hypertrophy of both sides with a widely patent foramen ovale the size of a shilling as the only lesion. This is the only case of which we know of real *morbus cœruleus* occurring in an adult as a result of uncomplicated patent foramen ovale. Slight clubbing was also noted in Kilduffe's² case of defect at the lower part of the septum (persistent ostium primum) and marked hypoplasia of the aorta. Cyanosis was present only as a terminal phenomenon, and the red cell count was 3,680,000. This patient had always been subject to dyspnoea and palpitation on slight exertion and the organs showed marked venous congestion, with enlargement of the liver.

Physical Signs.—(a) *In Cases Uncomplicated by Mitral Stenosis.*—In the series of 60 cases of auricular septal defect here studied, this was complicated in 12 cases by a mitral stenosis, which alters the clinical picture. This leaves 48 cases of uncomplicated auricular septal defects analyzed, of which 24 were cases of "pure" patency, 9 of defect *above* the site of the foramen, and 12 at the *lower* part of the septum. Physical signs may be *absent* and this is especially true of defects at the *upper* part of the intraauricular septum (persistent ostium secundum); but in widely patent foramen ovale, a sufficiently characteristic murmur is usually present and sometimes a corresponding precordial thrill. Defects at the *lower* part of the septum (*persistent ostium primum*) are usually associated with extensive deformities of the auriculo-ventricular cusps, and the murmur produced is often best heard at the apex, and is "con-

¹ *British Med. Jour.*, 1873, i, 333.

² *Am. Jour. Med. Sci.*, 1914, 147, 880.

fused" or "roaring" in character and presystolic or systolic, or varying between these two phases. The murmur was associated, in 3 of the 12 uncomplicated cases of this type, with a *thrill* which accompanied a murmur heard "all over the chest wall" (Norman Moore), "at the junction of the upper and middle thirds of the sternum, a loud twanging sound" (Peacock), or "at the apex" (Kilduffe). In 6 others of our 48 cases of auricular septal defect uncomplicated by mitral stenosis, a thrill was present, that is, in 9 cases in all. Five of these were in "primary" patency, one being that by Abbott¹ cited above, and another, (Lesieur, Froment and Cremiere²) was in a man aged fifty-eight years with a patent foramen 3 x 4 cm. wide, who presented "an intense rasping systolic murmur heard over the whole precordium," and a thrill which "began faintly in presystole and increased during systole to an intense vibration." In the ninth instance, reported by Greenfield, where the opening lay in the extreme *upper* part of the septum, a presystolic thrill at the apex was accompanied by a "rough purring presystolic murmur followed by a blowing systolic one in the same area. A loud blowing systolic murmur replaced the first sound at the pulmonary area and later at the third left interspace." In another case reported by Villaret, Chauveau et Bariety,³ (not included in our series), there was a loud systolic murmur localized at the third left interspace with a slight, inconstant thrill; the auricular septum presented five perforations below a widely patent foramen ovale, and the authors argued that these signs were diagnostic of the defect, and were especially liable to be produced by *multiple* defects, from vibration of the imperfect septum.

In *widely patent foramen* the *murmur* may be systolic or presystolic or may change from one to the other; it may begin in presystole and continue into systole, or two independent murmurs may occur. Tillbury Fox (1859) first noted the possibility of a presystolic murmur synchronous with auricular systole in patent foramen, and Eichhorst speaks of a presystolic murmur with maximum intensity at the level of the third and fourth interspaces, and makes the observation that these are intermittent phenomena which occur only when pressure in the right or left auricle is exceptionally raised so that the current passes with extreme force from one to the other. A presystolic element was present in 17 of our cases of uncomplicated auricular septal defects and in 16 cases of patent foramen collected by Gignoux,⁴ 8 of which are not included in our series, making 15 cases on record of presystolic murmur in this condition. In quality the murmur is sometimes soft, but may be harsh and rasping, or of a peculiar blowing or even musical character, and may be localized in the second, third, or fourth interspace near the left sternal border, or over the midsternum or right sternal border in this situation, or it may be diffusely heard over the precordium. *It is frequently audible in the left back*, and may be transmitted to the apex and axilla, or (occasionally) to the left subclavicular region or may be heard loudly over the whole chest. Among the 24 cases of "pure" patency in our series, such a murmur

¹ *Bull. Int. Méd. Mus.*, 1916, vol. 6.

² *Lyon Méd.*, 1916, 116, 1045.

³ *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1926, 42, 460.

⁴ *Deutsches med. Wchnschr.*, 1895, 21, 870.

occurred 20 times; in 16 cases it was systolic, and in 4 of these it was accompanied by a diastolic murmur; in 7 others the murmur was presystolic, which in Moul's case ran into systole, in that by Abbott was associated with a harsh systolic murmur and a presystolic element at the right sternal border; in a third (Ohm) was inconstant, varying from presystole to systole and in intensity also; and in the fourth was limited to presystole (Johnson). In one case only of our series was the murmur *mid-diastolic*, that by Bard et Curtillet, who described a "peculiar blowing diastolic murmur in the third left interspace near the left sternal border of moderate intensity."

The fact that both *murmur and thrill may vary both in intensity and rhythm* with the position of the patient or on different occasions, being presystolic or systolic at different examinations, is an important diagnostic point (Ohm).

When an *organic mitral insufficiency* is combined with a patent foramen, the regurgitation of blood through the defect into the right auricle during systole of the ventricles may give rise to a *positive venous pulse* in the neck, without the presence of tricuspid insufficiency. This was pointed out by Reineboth¹ in the case of a defect in the upper part of the septum "the size of a two-mark piece" lying a short distance below the foramen ovale which also showed a valvular patency, in a man aged forty-six years. When mitral stenosis is also present this sign is likely to be of no value on account of the auricular fibrillation so commonly associated.

(b) *Cases Complicated by Mitral Stenosis.*—*Auricular septal defects are not infrequently associated with mitral stenosis*, and this occurred in 12 of the 60 cases analyzed here, of which 8 were in simple patency of the foramen ovale, 3 in *persistent ostium primum*, and 1 in defect at the extreme upper part above the site of the foramen. This combination of mitral stenosis and auricular septal defect presents a well-defined clinical picture. The cases usually run their course under the guise of the complicating valvular lesion, but the defect introduces a definitely favorable condition in that it provides a way of escape for the blood in the left auricle which would otherwise be dammed back upon the pulmonary circulation, but which now passes either into the pulmonary artery, overloading that circulation, or, as compensation fails, throws the strain of the increased pressure back upon the less vitally placed systemic circulation. That the coexistence of these two lesions is a fortunate coincidence was pointed out by Firket (1880), in reporting the first case on record, of a woman with mitral stenosis who reached the age of seventy-four years after passing successfully through 11 pregnancies and 3 abortions, and by Lutembacher² (1916), in a woman whose heart presented a patent foramen 3.5 x 4 cm. wide and a mitral orifice reduced to a mere chink, who went through 7 pregnancies without any sign of failing compensation, and died at the age of sixty-one years, with marked terminal cyanosis; and it is shown also by the high age at death of the cases reported by Bonnabel (2 cases aged seventy-four and sixty-two years), by Wagstaffe³ (fifty-two

¹ *Deutsches med. Wchnschr.*, 1895, **21**, 870.

² *Arch. Mal. du Cœur.*, 1916, **9**, 235.

³ *Trans. Path. Soc.*, London, 1853, **19**, 96.

years), and 2 cases by Tylecote¹ (fifty-two and forty-three years). A remarkable case of this combination was reported by the writer.² The patient was a married woman aged thirty-eight years, admitted with auricular fibrillation and a hugely dilated right heart, who gave a history of repeated attacks of rheumatism and presented a hemiplegia of some years' duration evidently due to a paradoxical cerebral embolism. The heart showed the signs of mitral stenosis with insufficiency but there was also a presystolic thrill at the left fourth interspace and a murmur audible toward the base apparently produced by the defect. The mild degree of cyanosis which accompanied the advanced stage of failing compensation increased at the end to an intense blue. At the autopsy a widely gaping foramen 2.5 x 1 cm. in size and *with calcified lower border*, occupied the margins of a hugely distended fossa and annulus ovalis, and the border of the latter on the side of the right auricle showed anomalous fenestration and other minor anomalies. Both auricles, especially the right, were enormously dilated, the latter in an almost aneurismal fashion, and the coronary sinus and veins were hugely dilated. In another case reported by Cramer and Frommel³ of a communication 3.5 x 2 cm. wide associated with an extreme degree of what was thought to be congenital mitral stenosis, the woman was a typical "Lorrain dwarf" and death took place at the age of forty-one years by failing compensation without any terminal cyanosis, ascribed by the writers to a primary asystole of the hugely dilated right auricle, *which latter had produced during life a definite dulness in the back between the scapulae*. Other cases of this combination are recorded by Dufour et Huber,⁴ Griffith⁵ Peacock⁶ and Söldner.⁷

This entire subject was reviewed recently by Lutembacher⁸ who proposed the term "*mitral stenosis with interauricular insufficiency*" for cases in which, in the presence of an advanced degree of mitral stenosis, a valvular foramen was forced into permanent patency by the raised pressure in the left auricle. The most valuable differential points from an uncomplicated mitral stenosis are supplied by the altered size of the left auricle which is here relatively little dilated and by the enormous hypertrophy of the right heart which produces a characteristic roentgen-ray picture of a magnified *cœur en sabot* due to the great hypertrophy of the right ventricle pushing the left border of the heart up and curving round it in convex fashion to form the apex. Other significant points mentioned by Lutembacher which do not yield the same positive evidence as is obtained from the roentgen-ray, are: (1) the *entire absence* of cyanosis except as a terminal feature; (2) the smallness of the radial pulse; (3) the characteristic murmur which is frequently absent but when present may be localized in the second or third interspaces near the left sternal border and heard over a fairly large area but not clearly transmitted. In E. Weiss' patient, the diagnosis was made during life from the following features in the roentgen-ray: (1) sabot shape; (2) small aortic shadow

¹ *Lancet*, September 19, 1903.

² *Bull. Int. Assn. Med. Mus.*, 1915, 5, 132.

³ *Arch. Mal. du Cœur*, 1923, 16, 560.

⁴ *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1911, 31, 56.

⁵ *Manchester Med. Chron.*, 1902, 4, 383.

⁶ *Tr. Path. Soc.*, London, 1860, 8, 142.

⁷ *Munich Thesis*, 1904.

⁸ *La presse méd.*, 1925, 33, 236.

indicating hypoplasia; (3) prominent pulmonary arc; (4) exaggerated hilum shadows; and (5) no left auricular prominence. An interesting feature was a paralysis of the left recurrent laryngeal nerve which was evidently caused by the greatly dilated pulmonary artery.

Moukhtar¹ reported a huge defect in the interauricular septum complicated by a large cardiac aneurism at the apex of the left ventricle from coronary thrombosis, in a woman, aged thirty-three years, who presented extreme cyanosis during the last five years of life and died with generalized anasarca. The right chambers were enormously dilated and he ascribed this and the marked decompensation to the cardiac aneurism which had reduced the aspiratory power of the left ventricle and produced an "interauricular insufficiency" (left to right shunt) as does a mitral stenosis (Lutembacher). The terminal cyanosis was the result of the failing right ventricle.

Causes of Death.—Among the 60 cases analyzed here, of the 12 cases complicated by mitral stenosis, death was ascribed to the *valvular* lesion in 10 cases, of which in 9 cases the cause was failing compensation and in 1 case a suffocative dyspnoëic attack. In the remaining 48 cases of uncomplicated defects of the interauricular septum, death was apparently directly due to the defect in 27 cases, in 17 of these to failing compensation, in 6 to dyspnoëic or convulsive attacks, in 4 to pulmonary and paradoxical embolism and in 1 to cerebral hemorrhage. In 4 others of the uncomplicated cases death was caused by bronchopneumonia.

Paradoxical Embolism.—A serious clinical significance is given to patent foramen ovale by the fact that particles may be carried through the defect from the venous circulation to the arteries of the brain, or from the systemic arteries to the lung, leading to instant death. This possibility was first pointed out by Cohnheim in an observation of a woman dying of embolism of the middle cerebral artery. The foramen admitted three fingers, the arterial system was clear, while the primary thrombi lay in the veins of the lower extremities. Ohm² collected 11 such cases from the literature in which an embolus from a thrombosed vessel or a metastasis from a new growth undoubtedly passed through the open foramen and added an original case. Ballet³ collected 6 cases of death from cerebral abscess from infected emboli in which both cardiac and cerebral symptoms were present during life. In 3 of these there was a patent foramen, in 2 a defect of the interventricular septum.

Versé⁴ also described 2 typical cases. In 1 of these, a man aged seventy years, an embolus 13 cm. long derived from the iliac veins lay astride a patent foramen ovale the size of a lead-pencil, one-half in either auricle; death occurred from pulmonary embolism, and a "crossed embolism" of the right cerebral artery, followed by a right monoplegia, had occurred four days earlier. A similar case and still more remarkable occurred in the experience of T. R. Elliott of London (Fig. 60). The foramen shows a slit-like valvular patency and is occupied by a slender embolus 11 inches

¹ *Bull. et mém. Soc. méd. d. hôp. Paris*, 1926, **42**, 1402.

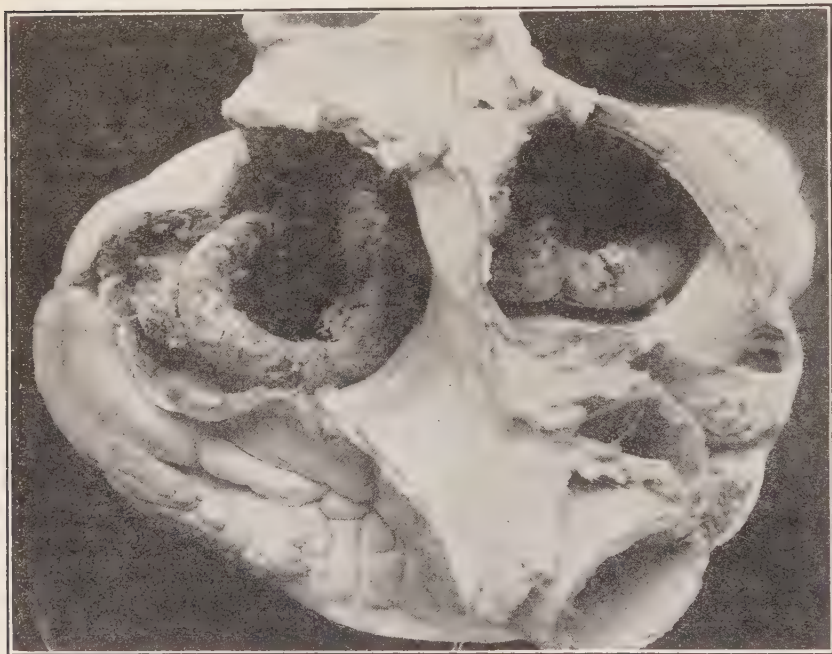
² *Zeit. f. klin. Med.*, 1907, **62**, 374.

³ *Archiv. gén. de méd.*, 1880.

⁴ *XIII Verhände. deutsch. Path. Gesell.*, 1909, p. 215.

long, the greater part of which lies coiled within the left auricle, while its proximal end is visible in the right auricle lying against the septum and disappearing through the foramen to its emergence on the left side. In Versé's second case, in a man aged fifty-three years, the foramen was patent to a lead-pencil and multiple embolic processes had occurred as follows: (1) extension along the pulmonary artery; (2) an embolus 17 cm. long lay in the aortic arch and passed thence through the innominate into the right subclavian; (3) an embolus lay in the right common carotid; (4) a recent infarction of the spleen.

FIG. 60



Thrombus from iliac vein lodged in foramen ovale (paradoxical cardiac embolism). A smooth-walled antemortem clot shaped like a great worm, 11 inches long and $\frac{3}{8}$ inch in diameter, is held by its middle in the patent foramen ovale with the free parts coiled up on either side of the auricular septum, in the cavities of the left and right auricles. From a woman aged thirty-five years, who died suddenly on the eighth day after excision of the spleen for hematemesis, anemia and splenic enlargement. Autopsy showed septic thrombosis of the splenic and other veins. Septic infarction of lung. The left internal iliac vein was plugged with antemortem clot. From a case in the service of Dr. T. R. Elliott, London. Specimen in the Museum of University College.

W. W. Beattie¹ reports 2 cases which appear to throw light on the course of events in paradoxical embolism in valvular patency. The first was a well-developed and well-nourished woman of about thirty years, who, nine days after an appendectomy had symptoms of pulmonary embolism and immediately after, two hours before death, turned suddenly quite blue

¹ *Bull. Int. Assn. Med. Mus.*, 1925, **11**, 64.

(*cyanose tardive*). At the autopsy only a slit-like opening of the foramen ovale, well guarded by the valvula foraminis ovalis, which extended 1 cm. beyond the anterior margins of the ring, was found. Both branches of the pulmonary artery were completely occluded by long coiled emboli; that in the right being 15 cm. long, and about 6 mm. in thickness and firmer than that in the left branch, though both had the appearance of ante-mortem thrombi, and were evidently derived from the right iliac veins which were overlaid by a small pelvic abscess; at the bifurcation of the aorta lay a long thrombus which completely occluded the right common iliac and extended up 10 cm. in the lumen of the abdominal aorta, and there was also a small embolus in a branch of the right renal artery. The systemic veins were perfectly clear and it was evident that both the aortic and renal emboli were of paradoxical origin and had emerged from the right side through the slit-like foramen, which must have remained closed under physiological conditions of the circulation, when the pressure was highest on the left side. In this patient, occlusion first of the left and later of the right main branches of the pulmonary artery had occurred, and the suggestion is made that the rise of pressure in the right auricle induced by the sudden obstruction of the pulmonary circulation from the occlusion of this by the embolism, had forced open the foramen and thus permitted the egress of emboli to the aorta and kidney. Such a sudden rise of pressure has been demonstrated experimentally by Haggart and Walker¹ (quoted by Beattie) who showed in cats that sudden occlusion of the left pulmonary artery leads to a sharp rise of the pulmonary arterial pressure between 121 and 267 per cent., and an immediate fall in the systemic pressure. This is of great interest in connection with the series of events traced here.

LOCALIZED DEFECTS OF THE INTERVENTRICULAR SEPTUM

The interventricular septum may be completely absent (*cor biatriatum triloculare*), or it may be rudimentary, represented by a falciform process growing up from the lower and anterior wall of the ventricle, or *localized defects* may occur. These usually lie at its base, and are relatively common in association with other anomalies, but are not frequent alone. Defects elsewhere than at the base, whether alone or in combination, are among the rarest of cardiac anomalies.

Defects at the Base.—The cases of congenital cardiac disease here studied have been drawn only from reliable sources, and all have post-mortem reports attached, which should make them a fair index of relative frequency. It is therefore of interest to note that among them, while defects elsewhere in the septum are exceedingly rare, "pure" defects at the base are commoner than is usually supposed, and, in combination with other defects they rank as the most frequent cardiac anomaly.

Statistical.—Among 850 cases of cardiac anomalies here analyzed, a localized defect of the interventricular septum occurred in 240 cases and

¹ *Arch. Surg.*, 1923, 6, 764, 783.

elsewhere than at the base in 15 cases, making a total of 255 cases of localized interventricular septal defect (or 30 per cent.). Of the 240 defects at the base, 54 were classed as the "primary lesion," and 186 complicated other anomalies. Similarly, of the 15 cases "elsewhere than at the base" 5 were "pure" *i. e.*, uncomplicated and 10 were associated with other anomalies. Of the 54 "primary" defects at the base, 8 were complicated by *Rechtslage* or dextroposition of the aorta, (and are so grouped in the chart), leaving 46 cases of "pure" defect at the base uncomplicated by any anomaly, except (in 9 cases), bicuspid or supernumerary or (congenitally) defective aortic or pulmonary valves, and (in 5 cases) congenital tricuspid insufficiency. Of the 186 cases of defect at the base complicating other anomalies, 95 were in cases of pulmonary stenosis or atresia, among which *Rechtslage* or dextroposition of the aorta occurred 62 times. In 36 of the other cases the defect was associated with transposition of the great trunks, in 14 with persistent truncus arteriosus and in 9 with communication between the base of the aorta and pulmonary artery or root of the right ventricle (defect of aortic septum). That is to say, in 154 cases of defect at the base of the interventricular septum complicating other anomalies, it was associated with an irregularity of development of the great trunks or of the septum between these. In the remainder of these 186 cases the septal defect appeared to be an independent arrest of development, a true "associated anomaly;" thus it occurred in 1 of the 13 cases of congenital rhabdomyoma charted (case by Hlava), in 2 associated with wide patency of the foramen ovale (Beattie, McIntosh) and in 1 of subaortic stenosis (Trevor), in 2 cases of coarctation of the aorta, in 1 with patent ductus arteriosus, and in 2 cases of right aortic arch; or it occurred in such conditions as mitral and tricuspid atresia (12 cases), as a compensatory development for the carrying on of the circulation.

Pathogenesis.—The occurrence in the same heart of a defect at the base of the interventricular septum, pulmonary stenosis or hypoplasia of the developmental type and dextroposition of the aorta is the commonest of all combinations in congenital cardiac disease. So frequent is the association that a causal connection between the three conditions is suggested and the question as to which might be the primary lesion occupied much attention among the earlier writers. Rokitsansky divided the interventricular septum anatomically into a part anterior and one posterior to the pars membranacea and classified defects at the base according as they lay (*a*) in the anterior, or (*b*) in the posterior part of the anterior septum, or (*c*) in the posterior septum. This is a grouping based on scientific principles in that the "anterior part of the anterior septum" is derived from the bulbus cordis and defects which occur here open into the conus of the right ventricle, so that, both embryologically and anatomically, the rare cases of defect in this situation belong in a somewhat different category to those lying in the "posterior part of the anterior septum." He pointed out further that the usual situation for localized septal defects is, in the great majority of cases, in the "posterior part of the anterior septum," that is, just anterior to the pars membranacea. He considered that non-inflammatory pulmonary stenosis, dextroposition of the aorta, transposition of the great arterial trunks, and defects at the base of the

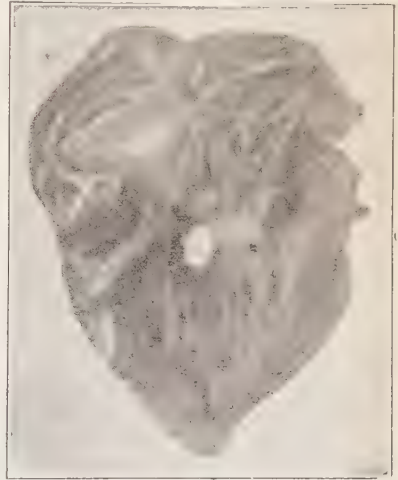
interventricular septum were alike dependent upon a common cause, which he believed to be a deviation of the aortic septum, which had resulted in an alteration in the relative size of the lumina of the two great trunks resulting in the non-union of the lower border of this with the interventricular septum, and believed that defects in this situation were practically always associated with a malposition of the great arterial trunks. Keith suggested that in the large number of cases in which a septal defect is associated with stenosis of the conus of the right ventricle, the defect is a direct result of the inadequate expansion of the bulbus cordis to form the infundibulum of the right ventricle. The theory that this combination of defects is due to a persistence of the reptilian right aorta has been noted.

Recent researches into the development of the critical bulbar region and pars membranacea septi have shown that the ventricular septum is not completed by a growth upward of this to join the aortic septum so that it comes to form a part of the aortic wall, as Rokitansky thought, but that the final separation of the two ventricles takes place by the fusion of the proximal bulbar swellings with each other, and with the right posterior endocardial cushion of the auricular canal (Frazer).

Independent defects of the interventricular septum in this situation, unassociated with any alterations in the relations of the great arterial trunks, and evidently not of inflammatory origin, may and do occur. This is so in the specimens in Figs. 61 and 62, and in cases reported by Orth,¹ Arnold, Preisz,² Hart³ and others. Such conditions cannot be explained on Rokitansky's theory as due to deviation of the septum, or, a deficient expansion of the infundibulum, but are the result, as Keith points out, of a primary arrest of growth of unknown origin. In Hart's case an interesting associated anomaly was an anomalous cord which extended from the lower border of the conus of the right ventricle through the septal opening, to the anterior segment of the mitral valve.

Pathology.—The commonest situation for the defect is directly beneath the aortic cusps and just anterior to the undefended space (Rokitansky's posterior part of the anterior septum) (Fig. 62a). Here it lies with the fleshy muscular septum before it and the thin pars membranacea behind,

Fig. 61



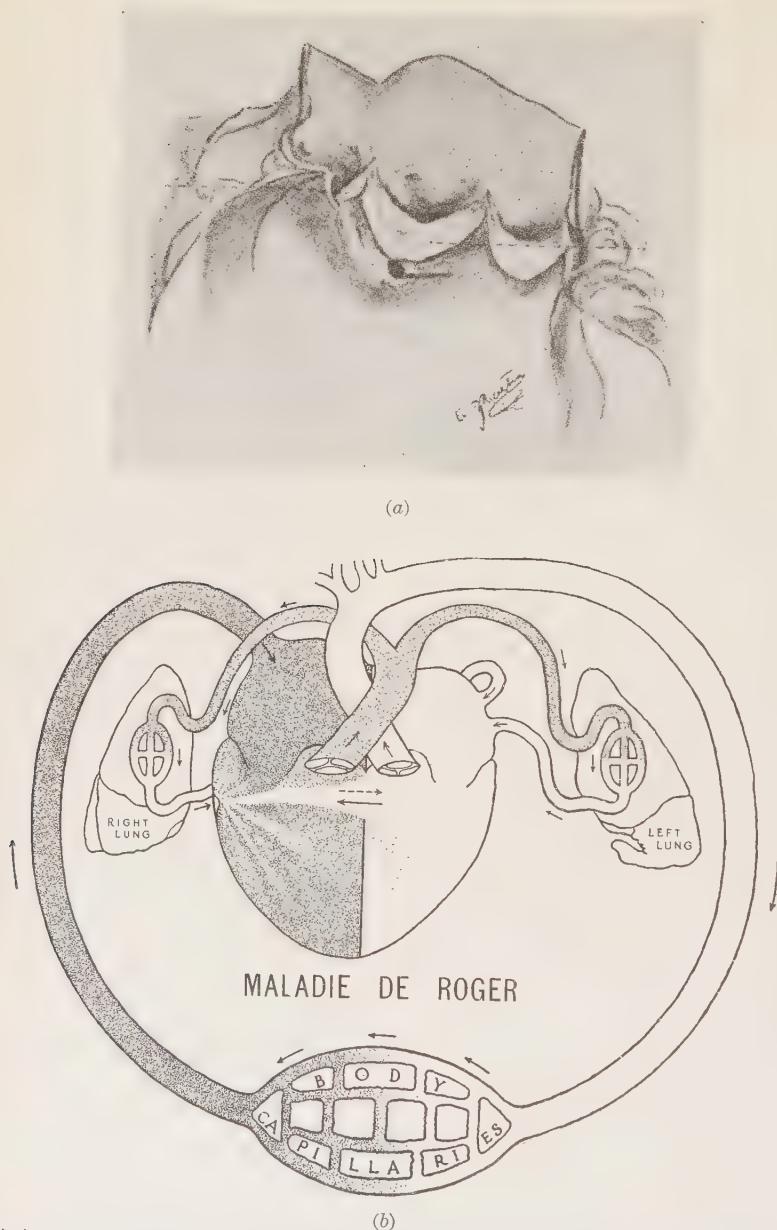
Defect of the interventricular septum at undefended space in the heart of an infant showing no other anomaly. View from right ventricle. (From a specimen in the McGill Pathological Museum, presented by Dr. John McCrae.)

¹ *Virchow's Archiv*, 1880, **82**, 529.

² *Ziegler's Beiträge*, 1890, **7**, 245.

³ *Virchow's Archiv*, 1905, **181**, 73.

FIG. 62



(a) Arterial-venous shunt. Localized defect of the interventricular septum just anterior to the undefended space (*Maladie de Roger*). From an adult subject, who presented no cyanosis, but characteristic physical signs. Outline drawing from a specimen in the McGill Museum, presented by Dr. John McCrae.

(b) Arterial-venous shunt in *Maladie de Roger* (localized defect of interventricular septum). The black arrow shows the direction of the current from left to right through the defect. The dotted arrow the course of the reversal current under a pathological rise of pressure on the side of the right heart. (From M. E. Abbott and W. T. Dawson, *Internat. Clin.*, 1924, vol. 4. By permission of Lippincott Company). Diagram by W. T. Dawson.

and opens in the right heart beneath the septal cusp of the tricuspid, sometimes perforating this or bulging the (adherent) tricuspid leaflet before it, or opening into the right auricle directly above the base of the tricuspid, thus establishing a communication between this cavity and the two ventricles. More rarely, the defect is placed farther forward in the septum in its anterior fleshy part, just behind the front wall of the heart, and is separated behind from the undefended space by a muscular column, opening into the conus of the right ventricle below the pulmonary valves, (Rokitansky's anterior part of the anterior septum). Examples are the cases by Coupland¹ and Rolleston.² In these cases, the defect is in the musculature of the interbulbar septum, *i. e.*, it is in that part of the interventricular septum which in the embryo formed the proximal part of the bulbus cordis before its division into the conus of the pulmonary artery and the vestibule of the aorta.

The defect varies in form and size from a pin-head perforation with tendinous edges, a round or oval hole admitting a goose-quill, knitting needle, index finger, etc., to a large triangular, semilunar, or crescentic space with thick-walled lower muscular border. Aneurismal pouching of the pars membranacea into the right ventricle may occur, with multiple sacculations perforated at their apices at one or more points (*vide infra*).

The margins of the defect with the adjacent valves and the mural endocardium in its neighborhood, especially on the side of the right ventricle, are very frequently invaded by an infective inflammatory process which becomes established here as the seat of strain leading to sclerosis and scarring, which act as a predisposing factor, both by vascularization of the tissues and by providing a nidus and crevices for the collection and multiplication of pathogenic bacteria when these are in the blood stream. Vegetations are commonly found fringing the margins of the defect, as in the cases reported by Whitley (1857) Callender (1858), Bennet, Horder and many others, and forming on the pulmonary valves, orifices, and conus luxuriant growths which appear to have extended upward from the defect. In a case recorded by Gordon³ of a boy aged five years with a congenital opening admitting a pencil between the ventricles, the pulmonary valves and adjacent wall of the right ventricle were the seat of a number of large grayish-green vegetations which extended below the level of the interventricular opening. Moschowitz⁴ related a similar finding in a woman, aged twenty-nine years, in whom the blood cultures showed *Streptococcus viridans*; there was a defect in the membranous septum admitting a lead-pencil. The pulmonary valves were replaced by large gray pedunculated vegetations, which extended up the wall of the pulmonary artery to its bifurcation, and had led to multiple emboli in either lung. In Whitley's⁵ case, a woman aged thirty-six years, who had always been healthy, symptoms of an acute infection with precordial pain set in nine weeks before death. At autopsy large vegetations the size of a marble were attached to the pulmonary valves and below this on the

¹ *Trans. Path. Soc. London*, 1879, **30**, 226.

² *Ibid.*, 1891, **42**, 64.

³ *Brit. Med. Jour.*, 1897, **ii**, 1174.

⁴ *Proc. New York Path. Soc.*, 1914, **14**, 18.

⁵ *Guy's Hosp. Repts.*, 1857, 3rd S., **3**, 255.

septal side of the conus were masses of vegetations closely adherent to the surface. Below the middle cusp of the aortic valve was a round opening admitting a goose-quill which passed into the right ventricle just above the attachment of the anterior curtain of the tricuspid valve. The orifice of the defect on the side of the right ventricle was covered with vegetations, as were both surfaces of the tricuspid valve.

Two of the cases reported by Horder¹ in 1908 had a very interesting localization in reference to the septal defect. In a man, aged thirty-one years, with history of rheumatism at twenty-four years, and of sudden onset of dyspnoea and precordial pain fourteen weeks before death, and a course of low intermittent fever with hematuria and albuminuria, the aortic valve was thickened and the seat of fungating vegetations and there was a hole in the membranous septum surrounded by a fibrous ring of endocardium and carrying a few small vegetations. *On the wall of the right ventricle opposite this hole there was a mass of fungating vegetations implanted upon a patch of thickened endocardium.* Recent infarction was found in spleen and kidneys. His other case was in a boy, aged seven years, with fingers somewhat clubbed, although no cyanosis was evident, who had a remittent fever for eight months. The ventricular septum presented a hole the size of a sixpence and there were many warty vegetations on the pulmonary valve which extended a little way along the pulmonary artery. Influenza bacilli were present in microscopic sections of the heart-wall and vegetations.

In a case reported by Hebb² of a girl, aged eighteen years, whose heart showed a funnel-shaped defect at the base of the septum admitting a goose-quill, there were large vegetations on the aortic, mitral, and pulmonary valves, and a *patch of vegetations was also situated on the wall of the right ventricle opposite the defect.* This observation, which is repeated in several other cases, as well as the frequent localization of the vegetations in the right ventricle affords an interesting proof of the fact that under normal conditions the current of blood flows from the left ventricle to the right through the defect. Further anatomical confirmation of this direction of the stream is afforded by the oblique direction and funnel-shape, with its larger end toward the left ventricle which the opening often assumes, and also by the not infrequent occurrence of *patches of fibrosis on the opposite wall of the right ventricle.*

Septal defects may exist without producing any change in the heart chambers, but they lead, still more frequently than do defects of the interauricular septum, to hypertrophy and dilatation of both ventricles. Where the defect is combined with *Rechtslage* of the aorta, marked hypertrophy of the right ventricle is a constant feature. The pulmonary artery may be markedly dilated, as in 19 cases of the 54 "primary" defects at the base.

The distribution of the auriculo-ventricular junctional bundle in septal defects is of much interest, and has been investigated by Keith, Mönckeb-berg, Morison,³ Grant and others. This bundle emerges from the auriculo-

¹ *Quart. Jour. Med.*, 1908-1909, **2**, 289.

² *Trans. Path. Soc.*, London, 1897, **48**, 41.

³ *Jour. Anat. and Physiol.*, 1913, **47**, 459.

ventricular node close to the interauricular septum behind the medial cusp of the tricuspid valve, and divides into two branches, the left of which pierces the interventricular septum just in front of the pars membranacea, and passes downward superficially beneath the endocardium of the septum to be distributed to the papillary muscles and columnæ carneæ of this chamber, while the right branch runs, more deeply imbedded in the musculature of the right side of the septum, to the apex of the right ventricle. In most of the cases of septal defect examined there was surprisingly little change in this normal arrangement, the fibres streaming over the free border of the septum that formed the base of the defect toward the apices of their respective ventricles. In Morison's case the left branch was abortive. Keith described an abnormal band of "sub-aortic musculature," which may develop in the pars membranacea and overlies the bundle as it courses down the surface of the septum in the left ventricle, and in one of Mönckeberg's cases of septal defect the bundle lay deeply in the musculature of the left septum instead of sub-endocardially as normally occurs.

In the complete investigation by serial section and reconstruction made by R. T. Grant on a malformed heart with absence of the interventricular septum (cor triloculare), from a cyanotic infant of fourteen months, who had presented during life a 2 to 1 heart-block, alterations were found in the branches *before* these had left the auricular region. A well-formed a-v. node was seen in its normal situation at the lower part of the auricular septum between the coronary sinus and the ventral fibrous body and from it two main strands of fibrous tissue passed to enter the dense structure of the central body. These strands, which were accompanied by bloodvessels, were extensively penetrated at this point, *i. e.*, before passing down to the muscular prominence at the back of the common ventricle which represents the rudimentary septum, by a network of fibrous tissue derived from the epicardium. It is suggested that division of the primitive atrial musculature from which the bundle is derived and which takes place at the level of the auriculo-ventricular cusps by ingrowth of fibrous tissue from the epicardium, had here been carried too far and that this had resulted in a certain degree of interference with and interruption of its fibres, resulting in the partial block that had existed during life.

Investigations by Flack and Mall have shown that the interventricular septum is formed, not by a process growing upward from below, as Rokitsansky supposed, but by a hollowing out of the spongy musculature of the embryonic ventricle to form the right and left chambers; the tip of the inferior septum, therefore, represents the wall of the lumen of the original cardiac tube, and this may account for the persistence of the bundle at this point in septal defects.

Symptoms and Physical Signs of Uncomplicated Septal Defects (Maladie de Roger).—We have differentiated two groups of localized septal defects according to the absence or presence of dextroposition of the aorta. This arrangement seems necessary for purposes of clear thinking along clinical and diagnostic lines, because the latter complication transforms what would otherwise be a pure arterial-venous shunt of the

circulation from left ventricle to right through the defect, into a venous-arterial one from the right to the left side, with (in this latter case) the result of raising of the oxygen-unsaturation of the blood and production of its symptom-complex of congenital cyanosis (compare Fig. 62a and b). We believe that the term "*Maladie de Roger*" should be applied only to the first of these groups, that namely of defects at the base uncomplicated by *dextroposition* or any other *malplacement of the great trunks*. Such cases supply more conspicuous examples of a continuous arterial-venous shunt of the anomalous current through the defect than any other septal communications, both because the opening (at the base of the septum) lies directly in the path of the raised systolic pressure in the left ventricle and because, from its situation at the root of the aorta, the defect is less exposed than is a patent foramen or patent ductus to the effects of alterations and fluctuations in pressure in the lesser circulation such as are occasioned by pulmonary or other complications and which might give rise to a temporary or terminal reversal of flow. The opening in an uncomplicated septal defect is also frequently extremely small, so that the amount of arterial blood admitted through it into the right ventricle with each systole is not sufficient greatly to overload the pulmonary circulation, as in the case of the huge defects not uncommon in the interauricular septum. The presence of such a localized septal defect is perfectly consistent with *complete functional efficiency* and the subjects may pass through life without any subjective manifestation of its presence, nor display any cyanosis except as a terminal phenomenon (and this only occasionally). Thus in the 46 cases of "pure" septal defect analyzed here an entire *absence* of cyanosis was noted in 24 cases, and in 7 others this feature was not mentioned, so it was probably negative; in 8 other cases cyanosis was "terminal," in 3 "slight," in 1 transient during attacks, and in only 1 case (Carpenter) was it said to be "marked."

On the other hand, the passage during systole of an anomalous stream of blood through this narrow channel at the base of the aorta gives rise, in the great majority of cases, to a prolonged and constant mesocardial systolic murmur usually heard best at the third and fourth left inter-spaces near the sternum and transmitted with diminishing intensity in all directions and heard usually in the back but not (in the uncomplicated cases) in the vessels of the neck. This murmur varies in intensity and harshness inversely with the size of the defect, being loudest and harshest in the medium sized and very small defects, and it is accompanied, in about one-third of the cases, by a purring systolic thrill (15 times in our 46 cases). A systolic murmur apparently produced by the defect occurred in 36 of 46 cases, and in 4 of these a diastolic element was associated and in 1 (Müller) a continuous humming sound. In only one of these cases was the murmur noted to be "absent." In the remainder the findings were either not recorded or were obscured by those of a concomitant valvular lesion. In the cases in which the character of the murmur was specified it was loud in 22, "rough" in 4, whistling, grating, sawing, each in 1, rasping in 3, harsh in 3; in 4 instances it was blowing. It was systolic in all 36 cases, and in 4 of these a diastolic and in 1 a continuous murmur was present as well. The point of maximum intensity was 12

times in the upper third of the precordium near the left sternal border; of these, in 4 it was stated to be at the third left space, in 2 others also at the fourth left space, in 2 at the third costal cartilage (in 1 of which it was heard with equal intensity at the apex), in 2 at the pulmonary cartilage and second left space, and in 1 "over the middle of the sternum opposite the third left interspace." Besides these, in 2 other cases it was "along the left sternal border," just to the left of the xiphoid cartilage," and "at the aortic cartilage;" in 2 it was "loudest at the apex," and in 4 it was diffuse over the precordium.

The murmur is usually transmitted downward along the left sternal border, and is frequently heard behind in the left infrascapular region. It may be diffused over the whole precordium, but is usually not heard in the axilla below the clavicle, or in the vessels of the neck. In 6 cases in this series it was so loud as to be heard over the whole chest, and in 2 cases it could be traced into the vessels of the neck.

These pronounced and arresting physical signs are in sharp contrast to the "*functional silence*" (Laubry and Pezzi) of the defect, which may come under observation with these objective manifestations in an otherwise perfectly normal young adult, who has perhaps presented himself for inspection for military or other reasons in the full flood of health and vigor. We owe the clear delineation of this distinctive clinical picture to a group of French writers, beginning with H. Roger¹ (1879), who in presenting a living case with this diagnosis, described as pathognomonic "a single long-drawn-out constant murmur beginning with systole and extending over both heart sounds with maximum intensity in the upper third of the precordium and presenting no other organic evidence except a purring thrill." Dupré² in 1891 published "the first case diagnosed during life and verified by autopsy" and proposed giving the name of "*Maladie de Roger*" to this syndrome. He described in a boy, aged four years with scarlatinal nephritis a "prolonged systolic murmur of remarkable force and harshness and a short systolic thrill with maximum intensity at the inner part of the third left interspace extending from here over the whole precordium and heard in the back but not transmitted into the vessels of the neck nor to the valvular orifices." During an attack of uremia the child developed a transient deep cyanosis "on slightest exertion" but the significance of this was not noted. Autopsy showed a small defect with tendinous edges 0.005 cm. in diameter and no other anomaly. The clinical picture of *Maladie de Roger* was completed by Reiss (1892) and Le Houx³ (1902) who pointed out in a series of illustrative cases (which include however some complicated by dextroposition) that a "late" or intermittent cyanosis although infrequent may occur in *Maladie de Roger*, just as in auricular septal defect, on the intervention of pulmonary complications or failing compensation. H. Müller⁴ (1920) reported 9 cases which illustrate admirably the distinctive physical signs in the absence of symptoms characteristic of the defect. Laubry and Pezzi observed that in these

¹ *Bull. de l'acad. de méd.*, 1879, 8, 1074.

² *Bull. de Soc. anat. de par.*, 1891, 5 ser. v, 404.

⁴ *Deutsches Arch. f. klin. Med.*, 1920, 133, 316.

³ *Thèse de Paris*, 1902.

defects the *cardiac sounds* are preserved in their integrity. and that the first sound may be lengthened by the force of the right ventricle, so that its closure gives an audible sensation resembling vaguely the rolling murmur of mitral stenosis; the second has similarly no reason to be weakened but on the contrary the pulmonary hypertension produces a resounding closure of the pulmonary valves, sometimes a little early, leading to a *pulmonary accentuation* or *reduplication*, and this may increase the resemblance to mitral insufficiency, with which lesion this defect is most often confused.

Radioscopy.—In the description by Vaquez and Bordet, the heart has a globular shape with marked convexity on either side and is a little increased in its horizontal diameter. Further as pointed out by Deneke the cardiac pulsations may be of an abnormal amplitude, and be seen along the left as well as right border, giving the impression of a “spherical pump.” The vascular arcs are normal. This description does not apply to the orthodiagraph in all cases of septal defect and certainly only when there is complete compensation; for, to again quote Laubry and Pezzi, it represents an equilibrium between the ventricles which is frequently broken. If this rupture is to the advantage of the left ventricle the silhouette will resemble that of a mitral insufficiency, if to the right that of a “right-sided lesion.”

Congenital Tricuspid Insufficiency.—In a certain number of cases the median cusp of the tricuspid valve, behind which a defect just anterior to the pars membranacea opens in the right ventricle, is involved in the defect, and is either congenitally rudimentary or bound down by inflammatory adhesions from a fetal endocarditis extending away from its margins. In either case a congenital tricuspid insufficiency will result, which early leads to cardiac insufficiency. There are 4 such cases in our series. One of these, reported by John Thomson,¹ is of an infant dying at two and a half years, and suffering throughout life from general weakness and inability to walk. Another by Gutzeit² (1922) was a married woman aged twenty-six years who was delivered in the middle of the seventh month with manual removal of an adherent placenta under ether. Three days later she had three attacks of dyspnoea and died. The right ventricle was dilated and greatly hypertrophied, and the pulmonary artery was dilated and atheromatous.

In a case reported by McIntosh³ two small defects lay just anterior to the pars membranacea, one of which opened into the right ventricle through a *greatly hypertrophied chorda tendinea*, which was attached to the much shortened infundibular tricuspid segment. The right ventricle was not dilated but somewhat hypertrophied. The margins of the defects were sclerosed and the venæ cavæ entered the right auricle by a common orifice. The defect was an accidental finding in a woman, aged forty-four years, dying of postoperative peritonitis.

Defects at the Base Complicated by Dextroposition of the Aorta.—In these cases the aorta appears displaced to the right and somewhat rotated on its axis, so that it rides over a large defect which lies just ante-

¹ *Edin. Hosp. Repts.*, 1894, 2, 292.

² *Virchow's Arch.*, 1922, 137, 358.

³ *Ann. Clin. Med.*, 1926, 4, 748.

rior to the pars membranacea and receives blood from both ventricles. The result is a direct passage of venous blood into the aorta and thence to the systemic circulation. This combination was reported by Dalrymple in 1847, in a cyanotic woman, aged twenty-five years, but the first complete study of this condition was made by Eisenmenger¹ (1897), in reporting a case, diagnosed by Schrötter before death, of a defect admitting the thumb in the posterior part of the anterior septum, with *Rechtslage* of the aorta and a dilated pulmonary artery. The patient, a man aged thirty-two years, had had cyanosis and dyspnoea from birth and some clubbing. There was visible precordial pulsation and bulging, and a systolic murmur over the middle of the heart transmitted everywhere over its surface, but chiefly to the right and inferiorly, not heard above its base, along the course of the aorta nor in the pulmonary artery, the latter vessel being too far below the surface to transmit the sound. It was argued that, in the absence of pulmonary hypoplasia, a free circulation would be permitted in this vessel and that therefore the murmur would not be transmitted along the aorta as Eisenmenger claimed should occur in septal defect complicated by *Rechtslage* with pulmonary stenosis.

An interesting case of this type has been communicated to us by E. A. Baumgartner. The patient, a delicately built young man, aged twenty years, with moderate cyanosis and presenting a loud systolic murmur over the heart with maximum intensity at the pulmonary area, and a soft diastolic murmur to the left of the sternum had suffered from hoarseness and aphonia from the age of thirteen years, and died of cerebral abscess (paradoxical embolism). The electrocardiogram showing an irregularity in the ventricular complex suggesting an abnormal distribution of the propagated impulse, and the roentgen-ray a greatly enlarged pulmonary arc. Autopsy showed a defect 2 cm. wide through which blood passed from both ventricles into the dextroposed aorta. The pulmonary artery and conus were hugely dilated and had probably produced pressure paralysis of the recurrent laryngeal nerve.

The symptomatology of defects of the interventricular septum with dextroposition of the aorta is well illustrated in the cases analyzed, for in 7 of these cyanosis of a moderate or marked degree existed, with, in 2 of the cases, clubbing of the extremities, the eighth case being in an infant, aged fifteen months (see Fig. 63a). In 6 of the cases also a loud rough or blowing systolic murmur was noted, localized over the precordium and accompanied, in 2 instances, by an apical systolic thrill.

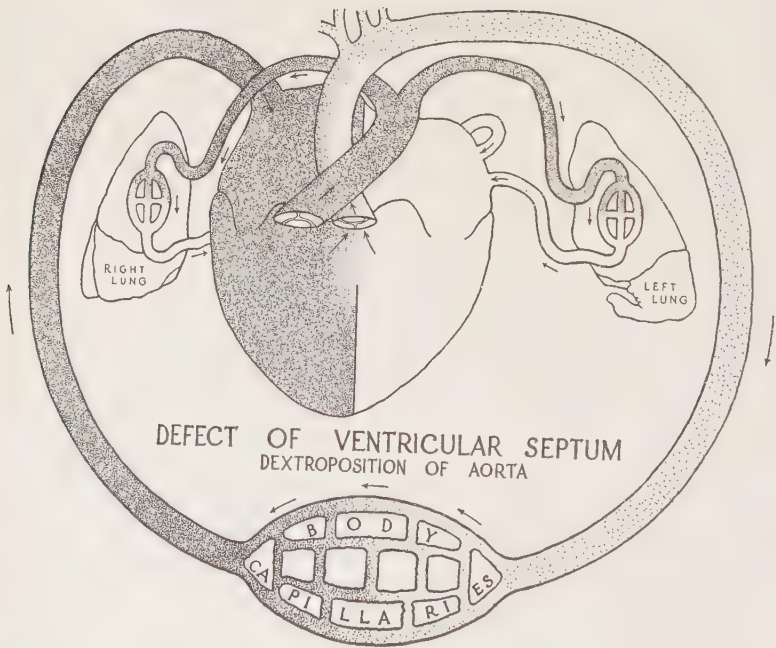
Causes of Death in Ventricular Septal Defects.—An analysis of the cases in this series gives interesting findings. (a) In *Maladie de Roger* the highest age attained was forty-four years, and the mean of the 46 cases was fourteen years. In 2 cases death was due to failing compensation apparently due to the lesion, but in both of these (Hebb, Carey) a congenital tricuspid insufficiency was associated. In a third case complicated by congenital tricuspid insufficiency death occurred in a dyspnoic attack; in a fourth case, an infant aged ten weeks, the child turned blue and died immediately after an operation for imperforate anus. In all the other

¹ *Zeitschr. f. klin. Med.*, 1897, 32, Supp. Heft, 1.

Fig. 63



(a)



(b)

(a) *Venous-arterial shunt.* Defect at base of the interventricular septum complicated by *Rechtslage* or dextroposition of the aorta, but without any pulmonary stenosis (Eisenmenger type). Note the twisting of the aorta to the right, so that it rides over the defect and the dilated pulmonary artery. (Specimen in McGill Museum, presented by Dr. G. Lomer.)

(b) *Venous-arterial shunt.* Diagram by W. T. Dawson, showing course of the circulation in defect of the interventricular septum complicated by dextroposition of the aorta. (From the article by Abbott and Dawson. By courtesy of the *International Clinics*.)

cases death was due to some intercurrent complication, which in 9 cases was bronchopneumonia, in 12 bacterial endocarditis and in 9 other infections.

(b) In the cases complicated by dextroposition of the aorta the highest age attained was thirty-three years, and the mean age of the 8 cases was sixteen years. Death occurred in 2 cases from failing compensation apparently due to the lesion, in 1 case from cerebral abscess, in 1 from bacterial endocarditis and in 1 from other infections.

Aneurisms of the Undefended Space.—Cases have been recorded by Rokitansky, Zahn,¹ Hart,² MacCallum,³ and others, in which, in the absence of any evidence of endocarditis, sacculations, single or multilocular, of the membranous portion of the septum project into the right auricle above the medial cusp of the tricuspid, and in some cases extend also into the musculature of the interventricular septum. Malignant endocarditis of the bulging area is not infrequent and rupture into the right auricle may occur. On this ground it has been argued⁴ that these aneurisms are not of congenital origin, but are due to the action of the inflammatory process upon this delicate part of the septum. As was pointed out by Rokitansky, however, the reverse is probably true, the aneurism supplying a nidus of lowered resistance upon which an infective process has been secondarily engrafted. This point was discussed by Mall,⁵ who pronounced definitely upon the congenital and non-inflammatory origin of these aneurisms, and shows the cause to be a malposition of the inferior septum so that "the membranous septum develops improperly and becomes placed in a horizontal position, and is thus weakened in every way, and predisposed to the formation of aneurisms." In his own case the membranous septum was cribriform, and the hole communicated with numerous sacs in the medial segment of the tricuspid, and also bulged into the right atrium.

Such aneurisms may give rise to marked and characteristic physical signs. This was true of two remarkable cases, one a heart which is in the McGill Museum, the other reported by Tate,⁶ in which a trumpet-shaped tube, which formed the apex of a saccular pouching of the pars membranacea, projected behind and perforated the medial cusp of the tricuspid valve; in the McGill specimen there was malignant endocarditis of the immediately adjacent tricuspid segment.

The relative frequency of *aneurisms of the right aortic sinus of Valsalva* and the probable dependence of these upon the juxtaposition of the pars membranacea of the right aortic cusp, has been discussed by Hart.⁷ The insertion of the medial cusp of the tricuspid just behind this point may further weaken this region by making it a seat of traction. This subject is further discussed below.

Defects in the Septum Elsewhere than at the Base.—These are usually multiple, and irregular or slit-like in form. They are of the greatest rarity. This is especially true of those low down in the septum. The

¹ *Virchow's Arch.*, 1878, **72**, 206.

² *Johns Hopkins Hosp. Bull.*, 1900, **11**, 69.

³ *Anat. Record*, June, 1912, p. 2921.

⁴ *Trans. Path. Soc.*, London, 1892, **43**, 36.

⁵ *Ibid.*, 1905, **156**, 51.

⁶ Buhl, *Ztschr. f. Biol.*, 1880, vol. **26**.

⁷ *Virchow's Arch.*, 1905, **182**, 168.

following case which appears to be unique in the literature, came under the observation of E. Weiss (personal communication). The patient was a man, aged seventy-nine years, with a marked systolic thrill and murmur pronounced near the xiphoid and an abnormal electrocardiogram. He had no heart symptoms throughout life but presented a *terminal cyanosis*, strikingly marked in the hands and feet. Photographs taken at the autopsy show a large round defect the size of a quarter dollar with sharp-edged fibrous margins, lying not in the usual situation but located nearer the apex and more posteriorly than anteriorly, which was open in its full extent, on the side of the left ventricle, but on the right side formed an aneurismal bulging communicating by multiple fenestrations in its floor with the cavity of the right ventricle near its apex.

COMPLETE ABSENCE OR RUDIMENTARY DEVELOPMENT OF THE CARDIAC SEPTA

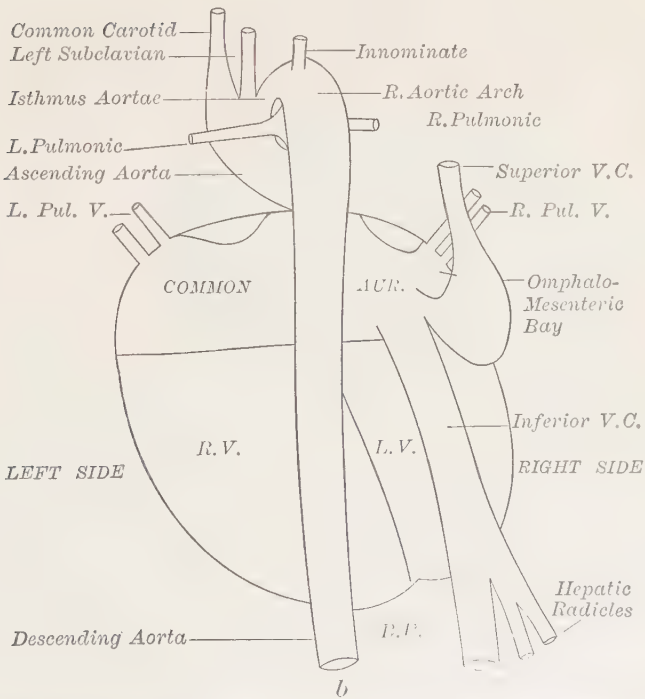
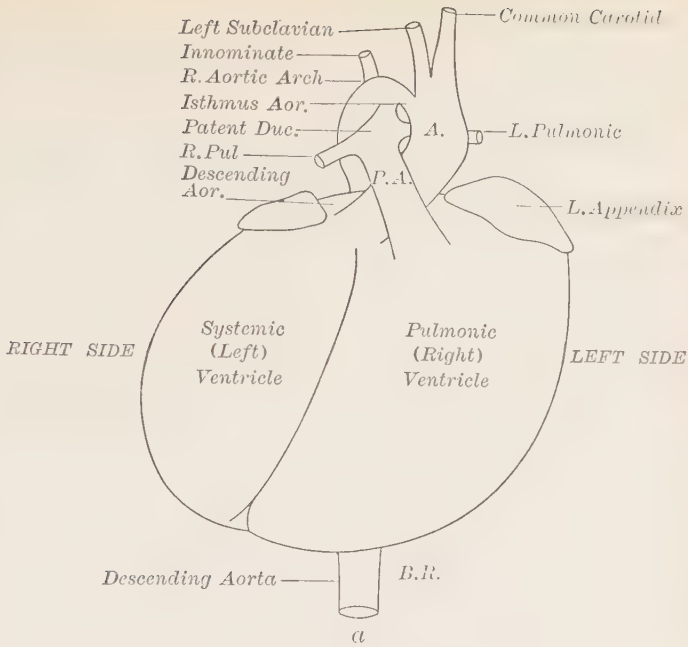
A rudimentary development of the cardiac septa, leading to a diminution in the number of the heart's cavities, should not be treated entirely apart from localized septal defects, being simply a more extreme degree of the same lesion. Yet the cases may be conveniently grouped together as indicating arrest at a very early stage of embryonic life (fourth week), frequently associated with anomalies elsewhere, and as forming an altogether different and more serious picture.

Cor Biventriculare Triloculare.—When the auricular septum is absent and the ventricular septum is present, a heart with two ventricles and a single auricle results. This condition does not in itself produce cyanosis, but since absence of this septum is usually due to maldevelopment of the pulmonary veins, it is generally associated with other grave anomalies and on this account the cases fall into the cyanotic group. Such a case is reported by Williams¹ in a cyanotic infant aged one month where all the blood entered the common auricle through the superior vena cava into which the left pulmonary vein emptied. The right pulmonary veins did not reach the heart but were rudimentary and formed an anastomosis in the right lung. The pulmonary artery was also atresic and dextrocardia existed. In a case reported by Bret Ratner and Abbott in a cyanotic infant, aged seventeen days, the great trunks were also transposed and a mirror-picture dextrocardia existed. The superior and inferior venæ cava entered the auricle together in a pouch representing a persistent omphalo-mesenteric-bay and the *right pulmonary veins entered low down on the right side of the common auricle*. There was a group of six accessory spleens. In a third case reported by M. G. Wohl,² in an infant, aged seven months, cyanotic since birth with clubbing, and a palpable thrill and systolic murmur over the precordium, the auricular septum was represented by a thin obliquely placed median strand. The *superior vena cava opened entirely into the left part of the auricle*, and the aorta and (atresic) pulmonary artery arose transposed from reversed ventricles. The spleen was absent and there were four accessory splenules.

¹ *Jour. Anat. and Phys.*, 1894, 28, 305.

² *Jour. Lab. and Clin. Med.*, 1925, 10, 812.

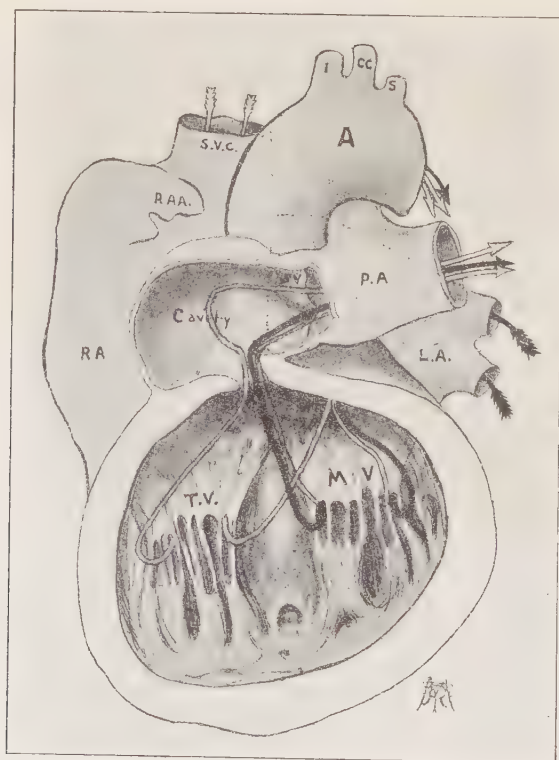
FIG. 64



Cor biventriculare triloculare with mirror-picture dextrocardia, transposition of the great trunks, displacement to the right of pulmonary veins and persistent omphalo-mesenteric-bay. From an infant, aged seventeen days under care of Dr. Bret Ratner, published with M. E. Abbott. *Am. Jour. Child. Dis.*, 1921, 22, 508. (a) Anterior view; (b) posterior view.

Cor Biatratrium Triloculare.—Absence of the ventricular with presence of the auricular septum constitutes a three-chambered heart with two auricles and the tricuspid and mitral orifices opening into a common ventricle, from which (if the aortic septum develops), two arterial trunks arise. Arnold¹ reports a case of complete absence of the ventricular septum, with auricular septum defective below (persistent ostium primum), pulmonary atresia, dextrocardia, and absence of the spleen, and adds a study of 30 cases of cor biatriatum triloculare. As in cor biloculare, obliteration of the right ventricle in tricuspid atresia (with auricular septum present) is frequently reported as triloculate heart.

FIG. 65



Cor biatriatum triloculare with malposed interventricular septum. Diagrammatic sketch by Prof. R. Tait Mackenzie, showing course of blood and relation of cavities in Dr. Andrew Holmes' case of displaced interventricular septum cutting off a small cavity which gives off the pulmonary artery. The pale line shows venous, the dark line arterial blood. (From the Medical Museum of McGill University.)

A special type of anomaly has been established, of what is functionally a cor biatriatum triloculare, although four chambers exist, by a series of cases recorded in which an anomalous septum cuts off from a common ventricle a small chamber which lies at the base of the heart and gives

¹ *Virchow's Arch.*, vol. 42.

off one or the other of the great arterial trunks. Such a case, reported and figured by Holmes,¹ in 1824, the specimen from which is in the McGill Museum, is represented diagrammatically in Fig. 65. The auricles, which were enormously dilated, especially the right, emptied their contents through their respective ostia into a common ventricle, which gave off the aorta behind and somewhat to the left and communicated through a diamond shaped opening in an anomalous septum with a small cavity at the right upper angle of the common ventricle which gave off the dilated pulmonary artery in its normal relation to the aorta. In eight other similar cases reported by Young,² Peacock,³ Rokitsansky (2 cases), Chiari, Thérémín (Obs. 43), Mills⁴ and Marchand,⁵ and in a specimen which the writer has had the privilege of studying in the Museum of the Harvard Medical School, the aorta arose from the small chamber in front and to the right, and the pulmonary artery from the common ventricle behind it, the two vessels being in transposed relations. It has been suggested by Keith that in these cases the anomalous septum is the persistent lower orifice of the embryonic bulbus cordis, but study of the McGill and Harvard specimens leads to the conclusion, that in these specimens, at least, the strong muscular wall with a large defect at its upper border through which the small cavity communicates with the large common ventricle, is simply the malposed interventricular septum itself, which has failed to unite with the aortic septum, and has been carried around to the right in the further development of the heart.

A third variation of trilobulate heart is presented by cases of mitral or tricuspid atresia with absent or defective auricular septum. In tricuspid atresia the ventricular septum has been developed, but a defect remains at the base through which the blood passes from the large left ventricle into the pulmonary artery through the persistent bulbus, the sinus of the right ventricle having become obliterated. An excellent example of the former condition (tricuspid atresia) is published by Robertson⁶ under the title, *cor biatriatum trilobulare*. The auricular septum was defective below (persistent ostium primum) and an anomalous septum, evidently the persistent right valvula venosa, crossed the right auricle from the Eustachian valve, and was inserted into the base of the interauricular septum at the site of the tricuspid orifice, which was here obliterated, *possibly as a result of the insertion of the anomalous septum at this point*. The great arterial trunks were transposed, the aorta arising from the persistent bulbus arteriosus of the obliterated right ventricle, which communicated with the cavity of the left ventricle by a defect at the base of the otherwise fully developed interventricular septum. In the case of tricuspid atresia reported by Hedinger,⁷ a woman aged fifty-six years, who showed no cardiac signs throughout life except that during pregnancy a transient cyanosis appeared when she was angry, died with severe symptoms of cardiac insufficiency setting in six months before

¹ *Edin. Med. Chir. Soc.*, 1824, republished by M. E. Abbott, *Montreal Med. Jour.*, 1901.

² *Jour. Anat. and Physiol.*, 1907, **41**, 190.

³ *Trans. Path. Soc.*, London, 1854, **6**, 177.

⁴ *Jour. Med. Res.*, 1923, **44**, 257.

⁵ *Verh. d. XII Deutsch. path. Gesell.*, 1908, p. 174.

⁶ *Lancet*, 1911, **180**, 872.

⁷ *Centralbl. allg. Path.*, 1915, **26**, 529.

death. The heart was greatly enlarged and the aorta and pulmonary artery arose transposed from what seemed to be a single ventricle. The left auriculo-ventricular orifice was large and the left auriculo-ventricular valve tricuspid, while the right opening was represented only by a scar. The pulmonary valves were fused and a stenosis existed; an aplasic right ventricle lay in the right wall of the big left (common) ventricle and communicated with this by an opening 2 x 1 cm. Aplasia of the left chambers in mitral atresia is described by Bernstein¹ and by Girauld and Tissier.²

Cor Biloculare.—Early cases were recorded by Wilson in 1798, Farre in 1814, Ramsbotham in 1846, and Forster in 1847, and there are six in the recent literature by Rudolf,³ Konstantinowitsch,⁴ Gierke,⁵ Schroeder,⁶ Jensen,⁷ and Rivet and Girard.⁸ We have had an opportunity of examining the specimen recorded by Rudolf, which is in the Museum of the Toronto University. The patient was a girl of sixteen years, undeveloped and cyanotic, who suffered from marked dyspnoea and died of pulmonary tuberculosis. The auricular septum was absent and a large right was divided from a smaller left auricular portion, with corresponding auricular appendages, by a slight ridge on the posterior wall. A single large bicuspid auriculo-ventricular orifice opened into the left side of a single ventricle which gave off a large aorta and a smaller artery from its right side, in transposed relations, and separated from the left part of the cavity by a shallow muscular ridge, which lay in the posterior wall and marked the site of the absent interauricular septum. The pulmonary orifice was stenosed. The cases by Gierke and Konstantinowitsch were identical with this, except that the great vessels were not transposed and in the former the pulmonary artery was atresic, in the latter the aorta. In other cases the development of the aortic septum was completely arrested and a common arterial trunk replaced the two great vessels.

An anomalous entrance of the pulmonary veins into the superior cava, innominate, hepatic, or other veins, instead of into the left auricle, was noted in Wilson's case, and in most of those recently reported. In that by Rivet and Girard, of a cyanotic infant aged twenty-five days with polycythemia, these veins formed a common trunk which ended in the lobus spigelii of the liver, and anastomosed here with the venæ cavæ and portæ. It seems possible that this anomaly may be the primary one, at least as regards the non-development of the auricular septum, for comparative anatomy shows that differentiation of the auricles is evolved during the formation of a pulmonary circulation.

Such cases of pure biloculate heart are extremely rare. A more common form is that in which the septa are partly developed, and an incomplete division has occurred into four cavities, the organ still remaining two-chambered in the exercise of its function (incomplete double

¹ *Proc. New York Path. Soc.*, 1906, N. S., 6, 29.

² *Bull. Soc. d'Obstet. de Paris*, 1910, 13, 420.

³ *Anat. Soc. of Gt. Brit. and Ire.*, November, 1899.

⁴ *Prag. Med. Wchnschr.*, 1906, p. 657.

⁵ *Deutsches. Arch. f. klin. Med.*, 1911, 205, 122.

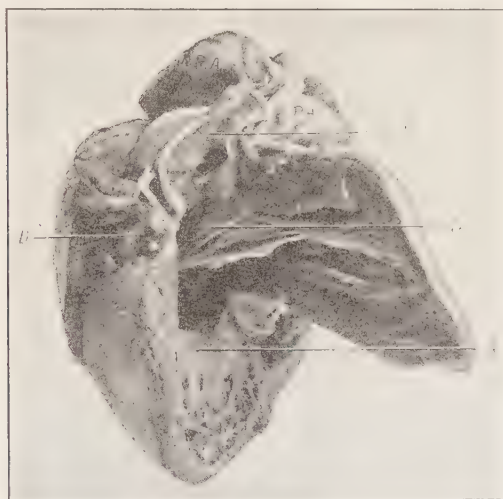
⁶ *Arch. des Mal. du Cœur.*, November 11, 1913.

⁷ *Charité-Annalen*, 1908, 32, 229.

⁸ *Giessen Thesis*, 1912.

heart). A good example is shown in a specimen in the McGill Museum, (Fig. 66). Here the auricles are incompletely divided into a large right and a small left chamber, by a narrow septum having a large defect above, multiple fenestrations, and a deeply concave lower free border (persistent ostium primum). A thick muscular septum, 1 inch high, with rounded free border, projects upward from the lower wall of the ventricle, partly dividing it into a small, thick-walled right, and a capacious left ventricle. A dilated aorta rides above this rudimentary septum and a narrow thin-walled bicuspid pulmonary arises from a rudimentary conus. There is a common auriculo-ventricular orifice with five cusps, one of which is very strong and large and arises from the opposing wall of either ventricle, stretching across above the rudimentary septum and shielding the auriculo-ventricular orifice from the two arterial ostia.

FIG. 66



"Incomplete double heart," showing (A) the interventricular septum, defective in its upper half; B, a large, thick-walled aorta, arising from both ventricles above the defect; C, a single auriculo-ventricular cusp arising from both ventricles; D, stenosis of the conus of the pulmonary artery; R.A., the enlarged right auricle. The right auricle and left ventricle are much hypertrophied and dilated; the left auricle and sinus of the right ventricle rudimentary. The interauricular septum is defective in its lower half. (From a specimen in the McGill Pathological Museum, presented by Dr. Andrewes.)

Biloculate heart is frequently displaced to the right side of the body, in that type of dextrocardia that is apparently due to arrest of development. It is often associated with transposition of one or more viscera or other serious defects. The spleen was absent in three of the cases.

Symptoms and Physical Signs.—In biloculate heart cyanosis is usually present from birth, and becomes very marked. The cases of Forster,¹ Ramsbotham,² and Crisp³ were all typical morbus cæruleus, dying, respectively, at seventy-eight hours, ten days and ten weeks. On the

¹ *Trans. Path. Soc.*, 1846, 1, 21.

² *Ibid.*, p. 21.

³ *Trans. Path. Soc.*, London, 1859, 10, 49.

other hand symptoms may be moderate, as in Turner's case, in which there was no cyanosis until just before death at the age of fifteen months. Cases of cor biatriatum trilobulare present perhaps the best illustrations we have that the admixture of venous and arterial blood is compatible with long life and with only slight disturbances of the circulation. Young's patient, who died at thirty-nine years, cyanosis having developed only within the last three weeks of life, and Peacock's almost identical case,

FIG. 67



Cor bilobulare with transposition of arterial trunks and patent ductus arteriosus. Situs inversus of stomach, duodenum, pancreas and spleen, partial situs inversus of liver and small intestine. The orifices of the transposed aorta, pulmonary, and common auriculo-ventricular opening lie in an oblique line from right to left downward. The aortic orifice lies to the right above and anteriorly. From a child dying of measles, aged eight and a half months. No cyanosis. (Case of Dr. Edward Weiss.)

already noted, and that by Mann,¹ dying at twenty-one years, are illustrations. Holmes' specimen (Fig. 65) was from a young man, aged twenty-four years, in whom there was only moderate cyanosis and a tendency to suffocative attacks. Physical signs may be prominent, but cannot be said to be characteristic. In a case of E. Weiss (Fig. 67) in an infant dying at eight months without any cyanosis, the autopsy showed a bilobulate heart with complete absence of auricular and inter-

¹ Ziegler's *Beiträge*, 1889, 6, 485.

ventricular septa and transposition of the great trunks with some hypoplasia of the pulmonary artery which had formed the descending aorta through the dilated patent ductus. There was also a partial situs inversus and a web-like obstruction of the rectum.

ABSENCE OR RUDIMENTARY DEVELOPMENT OF AORTIC SEPTUM

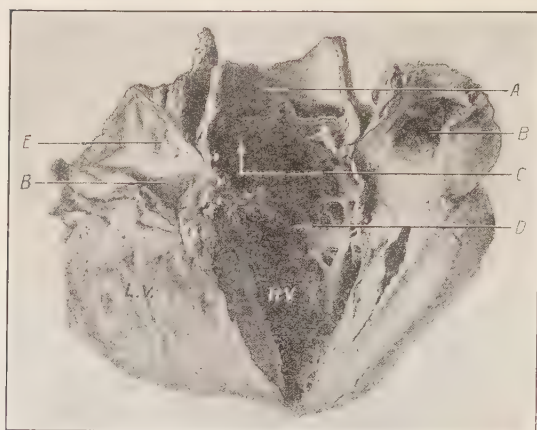
When the aortic septum fails to develop, a single large thick-walled trunk (*persistent truncus arteriosus*) results, which arches upward in the course and gives off the branches of the normal aorta, the pulmonary artery arising therefrom. This abnormality is very uncommon. Partial defect of the aortic septum is even less frequent than is its complete absence. It may result in a common trunk with early division into aorta and pulmonary artery and rudimentary septum within it, or, when the defect is still smaller, in an abnormal communication between the aorta and the pulmonary artery or the conus of the right ventricle.

Persistent Truncus Arteriosus (Common Arterial Trunk, Complete Defect of the Aortic Septum).—This abnormality is very uncommon, only 23 cases are available in the literature and from other sources of study. The cardiac septa are frequently rudimentary or absent, a biloculate or triloculate heart existing. When, however, these are well developed and the heart is four-chambered and otherwise normal, a localized defect at the base of the interventricular septum always remains. The common trunk either rides above it, receiving the blood equally from both ventricles, or arises more or less entirely from the right ventricle, the blood entering it from the left through the defect. This recalls the early stage at which the arrest of growth has occurred, when the primitive aorta is given off entirely from the right side of the common ventricle. A typical specimen illustrating this is shown in Fig. 66 from a specimen in the McGill Museum. The large common arterial trunk springs entirely from the right ventricle, and has three strong semilunar cusps, behind two of which the coronaries arise. Below the anterior and right posterior cusps there lies a circular defect in the septum, admitting the little finger, with rounded edges, by which the left ventricle communicated with the aorta and with the right ventricle, which is much hypertrophied; a heavy muscular column runs from the anterior wall of this ventricle to the lower border of the defect. The left auricle and ventricle are perfectly formed, but are much smaller than the right chambers. There are multiple defects in the interauricular septum. The blood supply to the lungs is unknown.

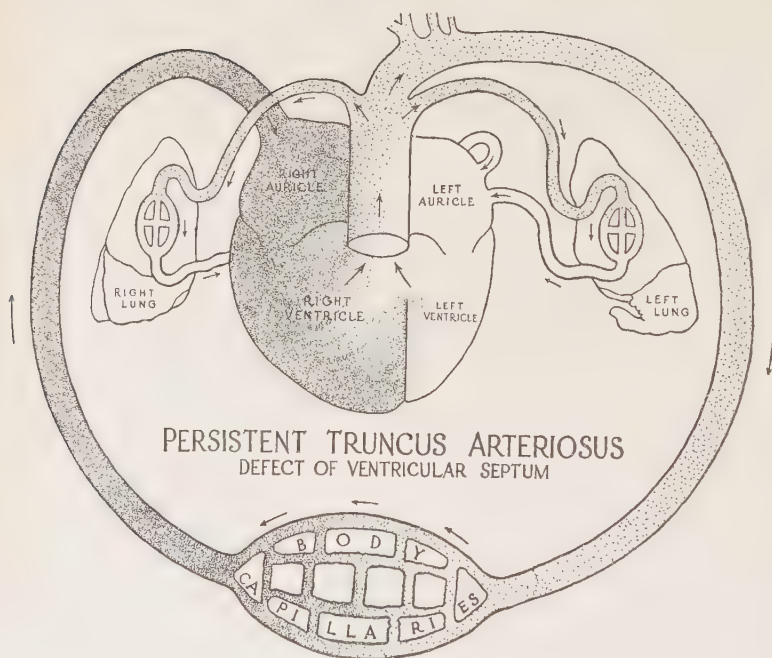
The pulmonary circulation in these cases is of the greatest interest. Two large branches, one to either lung, may arise from the wall of the common trunk some distance above its origin, as in the cases of Heath¹ and Ramsbotham. Quite commonly one pulmonary branch arises from the aorta soon after its origin, and supplies either the right or the left lung, and a second branch passes to the lung of the opposite side from the descending aorta, the first vessel evidently representing the pulmonary

¹ *Trans. Path. Soc.*, London, 1864, 12, 62.

FIG. 68



(a)



(b)

Venous-arterial shunt.

(a) Persistent truncus arteriosus. Heart of a child, aged five years, in whom cyanosis developed at one and one-half years. A, common arterial trunk arising entirely from right ventricle, and communicating with the left ventricle through the defect; B, right auricle laid open; C, defect at base of interventricular septum; D, heavy muscular column to base of defect; E, interauricular septum seen from right auricle showing multiple defects. (From a specimen in the McGill Pathological Museum presented by Dr. Mackenzie Forbes.)

(b) Diagram by W. T. Dawson, showing course of circulation. (By courtesy of the *International Clinics*.)

portion of the truncus (sixth aortic arch) and the second the patent arterial duct. This occurred in Dickson's¹ and Wirth's² cases, and also in that by Preisz.³ In the latter, distinct traces of a partial development of the aortic septum were apparent. A common trunk provided with four semilunar cusps, 14 mm. in diameter, arose from the right ventricle above a large septal defect, and widened rapidly to 3 cm., becoming grooved externally to indicate the right and left portions of its lumen, that part on the right giving off the vessels of the arch, and thus representing the aorta, while that on the left yielded the vessels to the right lung and represented the pulmonary artery. An additional pulmonary artery was here also sent to the lungs from the descending aorta in the position of the ductus arteriosus.

In a few instances in which the defect in the aortic septum appears to be only partial, the common trunk divides immediately after its origin from the heart, two-thirds of its lumen on the right forming the aorta, and one-third on the left forming the pulmonary artery, which takes its normal course.

This early division occurs in both of Rokitsky's cases, and in them the partial character of the defect is also proved by the presence of a delicate sickle-shaped septum within the undivided portion of the trunk, joining its wall between the left and posterior semilunar cusps behind, and left and right cusps in front. In Clarke's⁴ case the trunk divided early, but there was no sign of a rudimentary septum within.

The above are examples of true *persistent truncus arteriosus*. Under this title is also reported a series of cases in which the single trunk passing from the heart, represents the greatly dilated aorta or pulmonary artery, as the case may be, and an atresic cord attached to the external surface of the heart *represents the obliterated origin* of the other vessel. In one of Farre's cases, for instance, and in one by Forster, the single large trunk represented the pulmonary artery, and "a single coronary vessel which descended from the concavity of the arch to the base of the heart where it divided into two coronary arteries" was evidently the aorta, which was atresic at its origin, and was connected with the pulmonary by a large patent ductus. In Crisp's case, on the other hand, the pulmonary artery was rudimentary, and the large trunk represented the aorta.

As pointed out by Gierke, and also by Wirth, such cases should be clearly distinguished from the true persistent truncus due to complete absence of the aortic septum. Where the interventricular septum is defective at its base, as it is in all these cases, there is a tendency for the aortic septum to develop irregularly, thus cutting off a narrow aorta or pulmonary artery, as the case may be, and the calibre of the smaller vessel is likely to become still further reduced in size by the passage of the bulk of the circulation into the larger trunk. For this reason obliteration of one trunk in biloculate heart where no interventricular septum is present, is a comparatively common event, and the cases should be sharply distinguished from a true defect of the aortic septum. Gierke

¹ *Jour. Anat. and Physiol.*, 1914, 48, 210.

² *Giessen Thesis*, 1912.

⁴ *Trans. Path. Soc.*, London, 1885, 26, 178.

³ *Ziegler's Beiträge*, 1890, 7, 247.

suggests that the presence of four semilunar cusps such as occurred in Preisz's case is positive proof of an undivided primitive arterial trunk, while the presence of three semilunar cusps such as occurred in the McGill specimen, his own, Dickson's, and Wirth's argues that development of the aortic septum had occurred and that obliteration of one or other of the vessels had taken place as a secondary event.

Symptoms and Physical Signs.—Much the same remarks apply to persistent truncus as to bilocular heart, for symptoms and signs are not always commensurate with the seriousness of the lesion. But here the condition is a still graver one and the average duration of life is much shorter. Crisp's patient, a girl dumb from birth, with only slight cyanosis and clubbing, lived to twelve years, Forbes' to five years, Peacock's to thirteen months, and Buchanan's, who had a four-chambered heart with defect at the base of the septum, giving physical signs but no cyanosis, to six and a half months; all the others were marked cases of *morbis cæruleus* and died at birth or in early infancy. Vierordt quoted one dying at sixteen and another at nineteen years.

PARTIAL DEFECTS OF THE AORTIC SEPTUM

A localized defect of the aortic septum may occur either in the form of (a) an opening between the aorta and the trunk of the pulmonary artery a short distance above the valves, or (b) a congenital opening or a thinning leading to a congenital aneurism may exist in the aortic sinus of Valsalva communicating with or protruding into the conus of the right ventricle or pulmonary orifice at or immediately above the level of its valves. These two conditions have a similar symptomatology but they differ somewhat both in embryological significance, pathological appearance and clinical course.

(a) **Communication Between the Aorta and Pulmonary Artery.**—A few cases have been described in which a circular or oval hole with perfectly smooth edges, and evidently not of inflammatory origin lies in the anterior wall of the aorta a short distance above the semilunar cusps, and leads directly into the pulmonary artery shortly above its origin. A valuable developmental study was made by Hektoen,¹ who gives a case of much interest and collected 9 others from the literature. An eleventh case was described by Moorehead and Smith.²

The effect produced upon the circulation by the abnormal communication between the two great vessels is the same as in a patent ductus arteriosus, but the two conditions are quite distinct and have an entirely different etiology. This lesion is not a patent ductus abnormally shortened so that aorta and pulmonary artery have been approximated, with an apparent hole as a result. It is a true defect, as is proved both by its situation, which is much nearer to the origin of both arteries than is the ductus, and by the fact that in several of the cases reported the ductus has been present as well. Neither is the defect of an inflammatory nature, as is well seen in the smooth condition of its edges in the cases of

¹ *Trans. Chicago Path. Soc.*, 1905.

² *Irish Jour. Med. Sci.*, 1922-1923, Ser. 5, 1, 545.

Girard and Wilks, and from the character of the combined defects in Fraentzel's case.

The abnormal opening is clearly a partial defect of the aortic septum, not at its junction with the interventricular septum, but higher up in its own substance, probably at the point where the distal bulbar swellings meet the aortic septum proper in the embryo.

Instead of opening into the pulmonary artery, the hole may lead from the aorta into the right ventricle as in the cases of Livingstone¹ and Cayla. In one of Hektoen's cases the anomalous opening led from the aorta into the right ventricle through a defect at the base of one of the semilunar valves. This, also, is a most interesting example of a defect of the lower (bulbar) part of the aortic septum.

A *communication* between the aorta and pulmonary artery of an *acquired nature* may occur in much the same situation as in the congenital form in aneurism of the base of the aorta from acquired disease. There is quite a large series of cases, especially in the earlier literature, which is reviewed by Brocq.² The congenital cases are to be distinguished from those due to perforation of an aneurismal sac by the smooth appearance of the edges of the opening and the healthy arterial wall. The physical signs produced are the same and are often of remarkable intensity. Gairdner³ reported a typical case, characterized by a continuous murmur.

The pulmonary artery was larger than the aorta in Wilks' and Rickards' cases, a little smaller in Fraentzel's and Girard's cases. Marked hypertrophy and dilatation of all the chambers of the heart, especially of the right ventricle, constantly results. In Girard's and Rickards' cases, in which there was no other cardiac lesion, the hearts weighed, respectively, 670 gms. and 23 oz. (651.8 gm.).

(b) **Congenital Perforation or Aneurism of the Aortic Sinus of Valsalva With or Without Associated Bulbar Septal Defect.**—In another group of cases the right anterior sinus of Valsalva of the aorta (right coronary) is the seat of an opening leading into a thimble- or finger-like process which projects into the conus of the right ventricle with a thin membranous wall which is frequently ruptured at its top presenting an acquired communication. In a number of the cases, the defect *above* the valve is associated with a second defect of the anterior part of the interventricular septum *below* this which is derived from the bulbus cordis. In Hale White's case a defect admitting a No. 10 catheter lay with thickened wall just below the right half of the anterior aortic cusp and the septum around it for $\frac{3}{4}$ inch was thin and translucent while the sinus of Valsalva above the cusp was expanded into an aneurismal pouch which had ruptured into the conus of the right ventricle. The author thought the whole septum separating the lower part of the aorta and the left ventricle from the right chambers was abnormally thin. Rickards' case differed from the others in that there was no aneurism above the aortic cusp but an actual congenital hole admitting the little finger with smooth round edges, funnel-shaped and passing from behind the right half of the

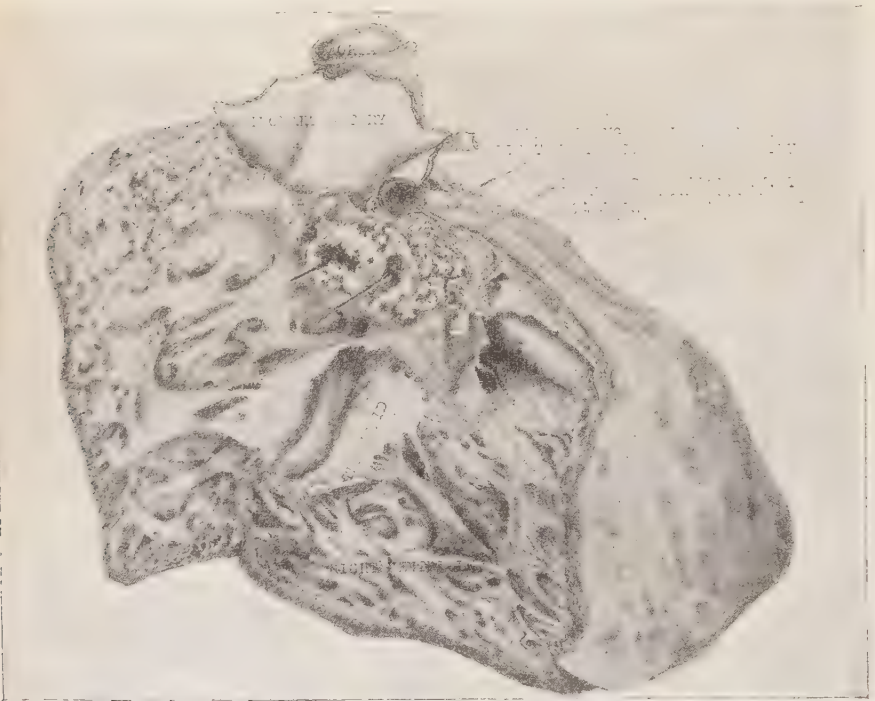
¹ *New York Med. Rec.*, 1883, p. 249.

² *Revue de méd.*, 1885, 5, 1046 and 1886, 6, 786.

³ *Glasgow Hospital Reports*, 1899.

aortic cusp into the right ventricle between the pulmonary cusps. In Beck's case a round opening in the large right aortic sinus led into a collapsed figure-like sac $\frac{3}{4}$ inch long projecting into the right ventricle between the pulmonary valves; and in that by Kraus just below the commissure between the right and left pulmonary cusps, the conus of the right ventricle was pushed forward by a membranous sac carrying on its anterior surface a diverticulum which was perforated in its floor. In the

FIG. 69



Interior of right ventricle showing trumpet-shaped ruptured aneurism and massive vegetations on wall of conus.

Ruptured congenital aneurism of right aortic sinus of Valsalva protruding into conus of right ventricle as a trumpet-shaped tube with associated defect of the interventricular (bulbar) septum directly below this. Extensive bacterial vegetative endocarditis of wall and margins of trumpet-shaped tube, and ventricular septal defect, aortic and pulmonary valves, and conus of right ventricle opposite and adjacent to the defects. From a man, aged thirty-one years. (M. E. Abbott, Osler Anniversary Volume, July, 1919.)

cases reported by Thurnam (1840), Charteris, Krzywicki, and in Hart's first case, no ventricular septal defect was associated, so also in the case published by Goehring, remarkable in that a congenital aneurism, thimble-shaped, and with thin walls, lay in the *posterior* sinus and ruptured into the *right auricle*. The pars membranacea was large and the aortic valve bicuspid. An infective endocarditis was associated in Thurnam's case and in Hart's third case, and in that reported by Abbott. The embryological explanation of the cases with combined defects *above*

and *below* the right aortic cusp is doubtless an arrest of development of the aortic septum at a stage figured by Tandler,¹ in which the distal bulbar swellings (which occupy the position of later semilunar cusps) have fused at the level of the valves before these have formed, while an aperture of communication still remains between the lumina of the aorta and pulmonary artery above, and the bulbar portion of the left and right ventricles *below*, the point of fusion. The homologue of such an arrest is probably to be seen in the foramen Panizzæ of the crocodile.

There are 11 fully reported cases of congenital aneurism or perforation of the aortic sinus of Valsalva in the literature. The subject has been studied by Hart,² Abbott,³ and Goehring.⁴ In my case (Figs. 69 and 70) a hollow tubular trumpet-shaped process 2 cm. long, which represents the ruptured aneurism, led from the floor of the anterior (right aortic) sinus of Valsalva, just below the orifice of the right coronary artery into the left ventricle between the two pulmonary cusps. The walls of this tubular opening were greatly thickened by an old inflammatory process, and were covered externally, and the margins of the tubular opening in the right ventricle were also fringed with long vegetations which covered also the walls of the conus opposite and adjacent to the defect in luxuriant fashion and also the thickened and insufficient pulmonary and aortic cusps (both surfaces of the latter). An ovoid defect 1 cm. long lay directly below this same right aortic cusp in the extreme anterior part of the interventricular septum, 1.5 cm. in front of the pars membranacea, and opened into the right ventricle immediately below the ruptured aneurism. Both pulmonary and aortic valves were insufficient from old inflammatory lesions and both left and right ventricles were greatly hypertrophied and dilated. The patient was a man, aged thirty-one years, with marked pallor of the surface and some dyspnœa but no cyanosis, who presented a prolonged diastolic almost continuous thrill over the precordium with maximum intensity in the second and third left interspaces, where it was so intense and superficial that the vibrations could be felt through the bed clothes and at some distance from the chest wall. It was accompanied by a very loud and harsh continuous murmur with diastolic accentuation interrupted only for a very short time in systole. The patient gave a history of sudden onset of these signs nine years before death when he was admitted to a hospital with a diagnosis of aneurism, and a correct ante-mortem diagnosis was made on the basis of this history and of the above findings.

Symptoms and Physical Signs of Localized Defects of the Aortic Septum.

—These are cases of an arterial-venous shunt of the circulation, for the pressure is as a rule higher on the aortic than on the pulmonary side, so that *cyanosis is usually absent*. The communication being, however, *above* the semilunar valves, the circulation through it is more under the influence of fluctuations in the arterial pressure than in defects in the interventricular septum, so that here, as in patent ductus arteriosus, a *tran-*

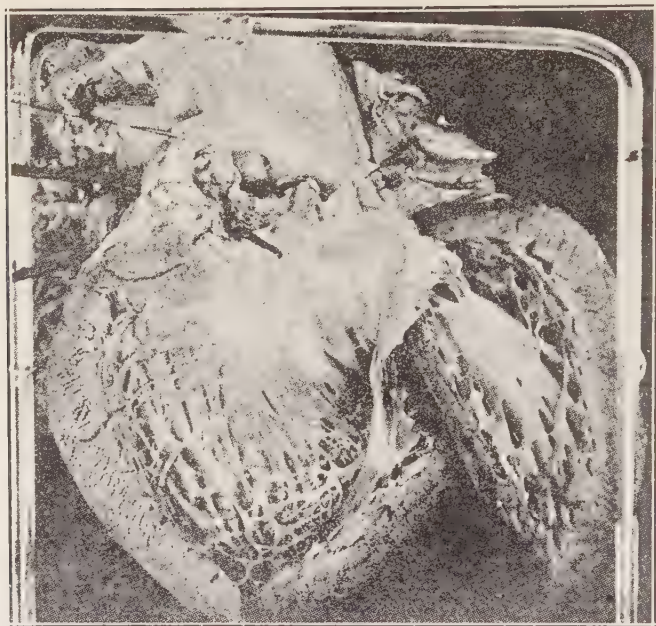
¹ Keibel and Mall's *Embryology*, vol. 2, Fig. 384, p. 552.

² *Virchow's Arch. f. path. Anat.*, 1905, 182, 167.

³ *Contrib. Med. Biol. Res.*, Osler Memorial, July 12, 1919.

⁴ *Jour. Med. Res.*, 1920, 42, 1.

FIG. 70



Interior of left ventricle showing defects *above* and *below* right aortic segment and bacterial endocarditis. From the case of congenital aneurism of right aortic sinus reported by M. E. Abbott.

FIG. 71



Interior of Model by Tandler showing bulbus cordis of embryo H_6 divided longitudinally. Showing a stage in which the distal bulbar swellings 1 and 3 from which the aortic and pulmonary cusps originally have fused to form the distal bulbar septum and proximal bulbar swellings (*p. Bw. A.B.*) have fused to form the portion of bulbar septum, and the septum aortico-pulmonale has grown downward for a short distance, leaving two points of communication between the aortic and pulmonary trunks immediately above and below the distal bulbar septum, aortic and pulmonary cusps (which are shown by this sound). *A.*, Aorta (4th aortic arch); *D. Bw.* 1-3, Distal bulbar swelling; *P.*, attachment of pericardium; *p. Bw.* *A. B.*, proximal bulbar swellings *A. B.*; *Pl.*, pulmonary artery (sixth aortic arch); *S.a.p.*, septum aorto-pulmonale; * point at which the sound of the lumen of the pulmonary artery disappears, being covered by the fusion of the distal bulbar swellings 1 and 3, forming the distal bulbar septum; ** point at which the sound again appears in the common lumen. The subdivision of the common efferent tube is produced distally by the septum aorto-pulmonale, in the middle region by the distal bulbar septum, and proximally by the proximal bulbar septum, between these three portions of the partition there are two points of communication, in which the ends of the sounds are visible." (From *Keibel and Mall's "Embryology,"* vol. 2, Fig. 384, p. 552.)

sient or *terminal* cyanosis is more likely to supervene from a temporary or final reversal of flow. This occurred in 7 cases among the 21 in our series, 4 of which were aortico-pulmonary communications and 3 of ruptured congenital aneurism, and cyanosis was otherwise absent in the entire group. Precordial pain, amounting to actual distress, was present from childhood in Rickards' case, as also in that by Fraentzel and Girard and in the two latter there were also dyspnœa on exertion with slight cyanosis. The sudden onset of these symptoms during later life, sometimes with a clear history of preceding physical strain, characterizes the cases of ruptured congenital aneurism and is an important diagnostic feature of this type of defect, as in Kraus' patient, who was convinced that his trouble began after lifting a heavy cannon ball. In Thurnam's case, a man, aged thirty-one years, symptoms of cardiac failure set in eleven weeks before death with a cracking sensation in the precordium, and in that reported by Goehring, a man aged twenty-two years, previously healthy, precordial pain, cough and dyspnœa set in one week before death and undoubtedly coincided with the date of rupture of the aneurism. Of the cases in our series of congenital aneurism the oldest was fifty-one, and the youngest fifteen years; they died of failing compensation (9 cases) or bacterial endocarditis (2 cases). Of the 10 patients with aortico-pulmonary communications those of Fraentzel and Girard died at thirty-seven and twenty-five years of failing compensation, that of Cesear at nine years of convulsions apparently dependent on an old cerebral abscess from crossed embolus, and the others in infancy.

Physical Signs.—In the rare cases in which a communication exists between the aortic and pulmonary trunks, physical signs are not constant and may be atypical, as in Girard's case, which was characterized by a slight thrill and systolic murmur at the apex which latter gave place later to a reduplicated first sound and gallop rhythm. Usually however, and always in communications between the aorta and base of the right ventricle or the pulmonary artery at its origin (as in all the cases of ruptured congenital aneurism), the signs are extremely forceful and significant of a communication between the two circulations directly underlying the chest wall. The sudden development of these dramatic signs and symptoms in a person previously in good health is pathognomonic of a ruptured aneurism in this situation which may very probably be of congenital origin. Owing to the great hypertrophy of the heart the cardiac dulness is increased especially to the right, and there is precordial bulging, and a prolonged systolic murmur or a continuous one with systolic, or systolic and diastolic, accentuation and an accompanying thrill widely diffused over the precordium and thorax but with maximum intensity at the second and third left interspaces, that is, lower down than the machinery murmur of patent ductus and lying closer to the ear of the observer. Sometimes, as in the writer's case, the prolonged murmur may be diastolic in rhythm, or continuous with diastolic accentuation, a fact which may probably be explained by the pulmonary insufficiency that coexists when the communication leads into the conus of the right ventricle.

TRANSPOSITION OR REVERSED TORSION OF THE ARTERIAL TRUNKS

Transposition of the Arterial Trunks.—This may be defined as an alteration in the position of the two great vessels relative to the ventricles of the heart or to each other at their origin, so that they either spring from reversed ventricles, the aorta from the right and the pulmonary from the left chamber (complete transposition), or from the ventricle to which they normally belong, but in a reversed relationship ("corrected" transposition).

The condition was first described by Baillie in 1797, and early cases were reported by Farre in 1814, Ward¹ in 1851, Peacock² in 1854, Buchanan³ and Meyer⁴ in 1857, Cockle⁵ in 1863, and Kelley⁶ in 1870. Thérémín found 26 cases of transposition among 106 cardiac defects. In his summary of the literature in 1898, Vierordt mentions 76 cases of transposition among 383 cardiac defects analyzed. Some 30 additional cases have been reported since. Among 270 cardiac defects in the London Museums examined by Keith, transposition occurred in 25. In our series of defects it was present 88 times.

Pathogenesis.—Peacock and others ascribed this anomaly to an irregularity in the development of the aortic septum, but until Rokitansky's work appeared in 1875, it remained a little understood phenomenon. In various particulars the observations of Rokitansky upon development do not coincide with those of later observers, but it is in the elucidation of the complex and hitherto obscure subject of transposition of the arterial trunks that the value of his great achievement chiefly lies. He had the singular triumph of having supplied a working hypothesis that has not only explained the facts of his own experience, but has outlined and foreseen other pathological possibilities which have since been realized. He described and figured sixteen different forms of transposition, due, he believed, to different degrees and combinations of deviation or malunion of the aortic and interventricular septa, some of which he himself observed, and others have since been recorded by later workers. Even if the advance of comparative embryology should unfold some other explanation of this subject, the verification of Rokitansky's brilliant hypothesis by the subsequent observation of different forms of transposition shown by it to be possible, indicates that, so far as it goes, his theory is true, and that growing knowledge will amplify rather than supersede his solution of this difficult problem.

Since the above statement was written for the first edition of this work, a remarkably clear exposition of Rokitansky's theory in the light of recent investigations upon the normal anatomy of the bulbus cordis in the dipnoan and reptilian heart and in the mammalian embryo, has been published by Jane Robertson.⁷ The following is a brief statement

¹ *Trans. Path. Soc.*, London, 1851, 5, 67.

² *Ibid.*, 1854, 6, 117.

⁴ *Virchow's Arch.*, 1857, 12, 364.

⁶ *Trans. Path. Soc.*, London, 1871, 22, 92.

⁷ *Jour. Path. and Bacteriol.*, 1913, 18, 191.

³ *Ibid.*, 1857, 8, 149.

⁵ *Medico-Chir. Trans.*, 1863, 46, 193.

of Rokitansky's doctrine of transposition, as corroborated and amplified by the result of these researches.

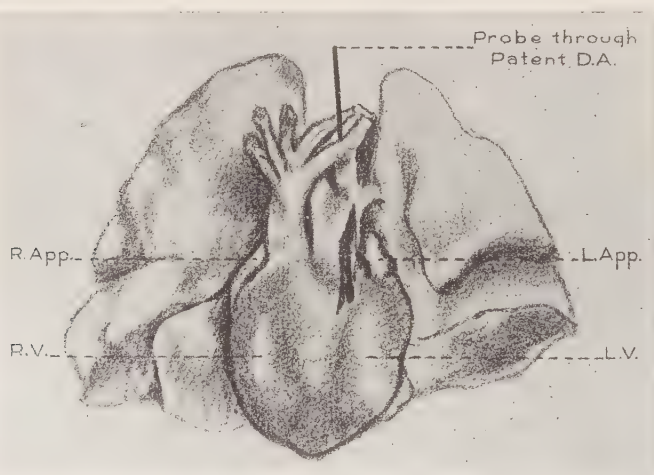
As may be seen by a glance at the normal adult heart, the great trunks normally undergo a distinct torsion upon each other just above their origin, so that the pulmonary artery, which arises in front and to the left, passes back behind the ascending aorta to the lungs, while the aorta, although coming to lie ventral to the pulmonary artery, springs from the heart behind it and to the right. This torsion of the vessels is represented in the bulbus cordis of the early embryo and in the dipnoan fish by a spiral arrangement of the valvular endocardial folds of the bulbus cordis, which results from a kinking upon itself of the bulbus, which structure was at an earlier stage a straight tube. The aortic septum is formed in its proximal portion by fusion of the spirally placed endocardial ridges of the bulbus cordis, and in its distal part by a growth downward of a septum in the common arterial trunk. If for any reason this normal kinking does not occur and the bulbus remains a straight tube, the aortic septum will not assume its spiral form, and the normal torsion of the great trunks upon each other cannot take place. The result is an aorta arising anteriorly and passing directly upward to the arch, and a pulmonary artery arising posteriorly and passing directly backward to the lungs, *i. e.*, *transposition*. In other words, transposition of the arterial trunks is due to a lack of development of the torsion that normally occurs. The transposed vessels may be placed in their proper ventricles in spite of their relative displacement, by the sympathetic adjustment of the aortic in its union with the interventricular septum. In this case the transposition is "*corrected*" (Rokitansky's Scheme A). Or the transposed vessels may be placed in the *reversed* ventricles by the union of the interventricular with the proximal portion of the malposed aortic septum, when "*uncorrected*" *transposition* results (Rokitansky's Scheme B).

Rokitansky recognized this spiral disposition of the aortic septum and taught that these two factors, a deviation of the septum within the aortic bulb and its faulty union with the interventricular septum, might occur in all degrees and combinations, giving rise to a corresponding number of different forms of displacement of the arterial trunks or of "*corrections*" of such displacements. His "Scheme A" has as its type or starting point the normal relation, in which the concavity of the septum looks backward and to the right. The characteristic of this group as a whole is that the interventricular unites with the aortic septum in such a way that, although the trunks are altered in their relation to each other, they remain placed in their respective ventricle: that is to say, the transposition is "*corrected*."

In his second group, or "Scheme B," on the other hand, the arteries arise throughout from the "*reversed*" ventricles, that is to say, the transposition is "*uncorrected*" in the union of the interventricular septum. The type, or fundamental form from which the series starts, is the so-called *transpositio vera*, in which the septum has rotated through nearly 180 degrees, so that its concavity looks downward and to the left, and the arteries lie in reversed cavities in the opposite of the normal position, the aorta to the left and anteriorly, the pulmonary to the right and posteriorly.

Another explanation of transposition has been offered by Keith, namely, that it is due to an atrophy of the bulbus cordis around the pulmonary artery, and its great muscular development about the origin of the aorta, where it normally undergoes involution. The effect would be the pulling round of the aorta at its orifice to the position normally occupied by the pulmonary artery, so that the relation of the two vessels to the auricular canal becomes reversed. A similar result would be attained by supposing a reversal of the normal right to left bulbo-ventricular bend, so that this undergoes a left to right twist, which would bring the vessel lying posteriorly into relation with the right side of the auricular canal. Such a reversal of the bulbo-ventricular bend has been suggested by Frederic Lewis and by Keith and such a reversed torsion in an embryonic heart at a very early stage is actually figured in Remak's atlas.

FIG. 72



Venous-arterial shunt. *Complete transposition of arterial trunks, aorta from right ventricle, pulmonary artery from left ventricle to the left of the aorta. Large patent foramen ovale. Large patent ductus arteriosus. Interventricular septum entire. Note the position of the pulmonary artery which lies to the left of the aorta and on the same plane, that is, is not completely reversed in relation to this.* (Drawing by Dr. Louis Gross from a specimen in the Museum of the College of Physicians and Surgeons, New York, presented by Dr. Pappenheimer. (M. E. Abbott and W. T. Dawson, *International Clinics*, 1924, 4, by permission of J. B. Lippincot Company.)

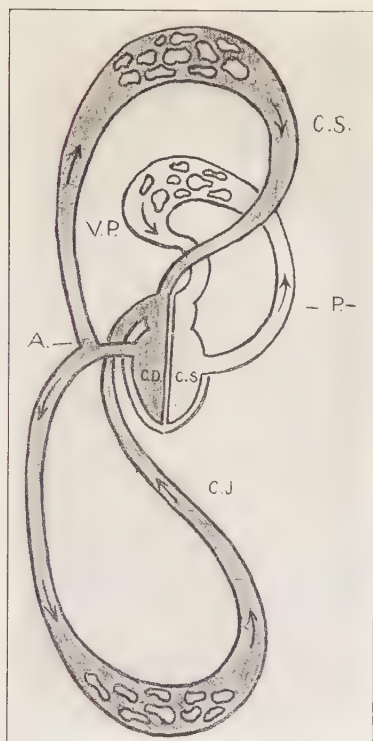
From a consideration of the above theories, and from the study of two models made by Dr. Frederic Lewis and myself,¹ the series of events occurring in transposition appears to us to be as follows: (1) A reversal of the bulboventricular bend, so that the two great trunks resulting from division of its distal aortic portion come to occupy a reversed relation to the auricular canal; (2) a reversal of the normal kinking of the aortic bulb so that it remains a straight tube or assumes a curve complementary to the reversed bulboventricular twist below; (3) a

¹ *Anat. Rec.*, 1915, 9, No. 1.

consequent reversal of the normal spiral arrangement of the bulbar endocardial ridges; and (4) a resulting malposition of the aortic septum so that its spiral twisting either does not take place, or takes place in a reversed direction, leading to a lack of the normal torsion of the great arterial trunks, that is, *transposition*.

The interdependence of the first and second of the above events is evident from a glance at the compensatory curves of the normal embryonic

FIG. 73

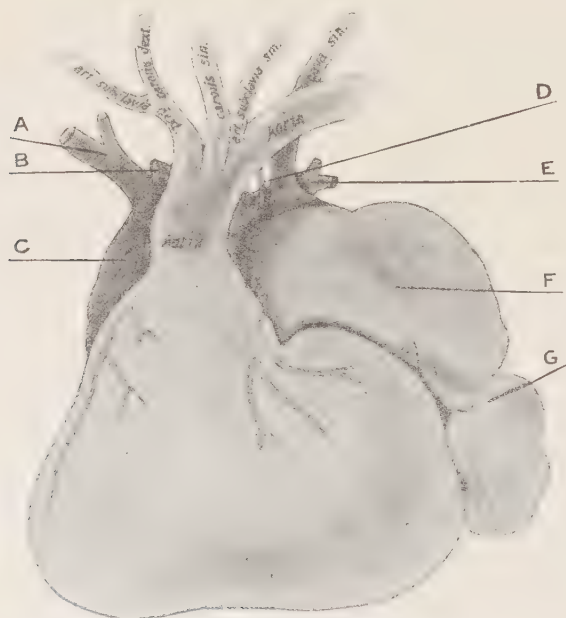


Circulation of the blood in transposition of the arterial trunks. The dark colored portion represents the venous blood, which is seen filling the entire systemic circulation, while the arterialized blood (uncolored) is confined to the lesser circulation. Communication through one or other of the fetal passages would be necessary for life. (Adapted from Bokay, *Arch. fur Kinderheilk.*, 1911, 55, 333.) C.S. *Cor sinistra*; C.D., *cor dextra*; P., pulmonary artery; A, aorta; C.S., superior cava; C.J., inferior cava; V.P. pulmonary veins.

bulbus (Fig. 39), but the question as to which of these two is of primary occurrence is not altogether clear. The reversal of the bulbo-ventricular twist may be of the nature of a localized *situs inversus* and the causative factor of the whole proceeding. Or it may be secondary to a primary arrest of the kinking that normally takes place in the aortic bulbus, and of the consequent lack of spiral disposition of its valves. That the second of these two alternatives, namely, a primary arrest of development, may be the correct solution is suggested in a striking

way by two remarkable cases reported by Wenner,¹ and Birmingham² of "pure" dextrocardia, in which the transposed vessels arose from the extreme right side of a common (in Birmingham's case of a right) ventricle, and *both auricular appendages lay entirely on their left side*, just as in the very early embryo, the common auricle lies to the left of the common trunk. In both cases the dextrocardia was not a true situs inversus, but the apex of the heart was formed by the right ventricle, again evidencing a persistence of an early embryonic state, and a true primary arrest of development.

FIG. 74



Wenner's case of cor biatriatum trioculare with transposed aorta and pulmonary artery passing up to the right, and both right and left auricular appendages displaced to the left side. A, Superior vena cava; B, right pulmonary artery; C, right auricle; D, ductus botalli; E, left pulmonary artery; F, right auricular appendix; G, left auricular appendix. (From *Beiträge zur Lehre der Herzmissbildungen*, Case 9. Otto Wenner, *Virchow's Arch.*, 1909, pp. 140, 155.

Pathology.—It is impossible to follow Rokitsansky's minute classification in a statistical study of recorded cases, for the relation of the vessels to each other is often indefinitely stated. For practical purposes the classification into complete, corrected, and partial transposition, suggested by Vierordt, may be used.

(a) In *complete transposition*, the vessels arise from reversed ventricles. This occurred in 58 of our 88 cases. In 18 of these the aorta arose from the right ventricle to the right and in front, and the pulmonary artery to the left and behind. The so-called *transpositio vera*, in which the

¹ *Virchow's Arch.*, 1909, 196, 127.

² *Jour. Anat. and Physiol.*, 1893, 27, 139.

aorta arises in exactly reversed relation to the left and anteriorly, and the pulmonary artery from the left ventricle to the right and posteriorly, is illustrated by the cases of Pye-Smith¹ and Thiele. The pulmonary rose above a defect in the septum and the aorta from the infundibulum of the right ventricle in three of Thérémín's cases, and in those of Lees and Rheiner. The aorta rose from both ventricles above the defect, the pulmonary from the left ventricle, in that by Buchanan.² The aorta arose from the right ventricle and was constricted at the isthmus, and the pulmonary artery formed the descending aorta through a widely dilated patent ductus in an infant aged six days recently reported by Dreyfuss,³ there was also a small defect in membranous part of the interventricular septum and a patent foramen ovale. In the case reported by Abbott and Dawson,⁴ of a cyanotic infant dying on the seventh day, there was a complete transposition of the arterial trunks and atresia of the aortic orifice just below the valves in the conus of the right ventricle, the myocardium of which showed extensive syphilitic degeneration. Here also the pulmonary artery formed the descending aorta through the dilated patent ductus, and was itself, with the left ventricle, hugely dilated.

(b) In *corrected transposition*, the relation of the vessels to each other is altered, but they are placed in their proper ventricles by the union of the interventricular septum. Minor degrees of displacement probably often pass unnoticed, for the "correction" prevents pathological results. More extreme grades can be at once recognized. Six almost identical cases are described by Rokitsky (2 cases), Rauchfuss, Tonnie,⁵ and Thérémín (2 cases), in which the aorta and pulmonary artery are completely reversed in relation to each other, but arise each from their own ventricle. In all there was a defect in the interventricular septum, at the base and in all *the auriculo-ventricular orifices were also transposed*, the mitral lying in the right, the tricuspid in the left ventricle, and thus the "correction" of the transposition of the arteries by the septum was seemingly nullified; the aorta arises from a ventricle of venous form (in that it has a tricuspid valve), the pulmonary from an arterially constructed one. Rokitsky suggests that in these cases "the ventricle in which the septum arises anteriorly forms as the arterial one." Fingerhuth described a case of corrected transposition with situs inversus of the viscera, and no transposition of the ventricles.

(c) *Partial transposition*, in which both vessels arise from the same ventricle or from a common ventricle in reversed relations, is relatively infrequent. *Both vessels may arise from the right ventricle*, as in Thérémín's forty-first observation and in Tooth's case,⁶ in which a large thick-walled aorta arose from the usual origin of the pulmonary artery, which was itself small, thin-walled, bicuspid, and was given off from the right ventricle directly behind the aorta. *Both vessels may spring from the left ventricle*. Thus, Crocker reported a girl, aged thirteen years, in

¹ *Trans. Path. Soc.*, London, 1873, **23**, 80.

² *New York Path. Soc.*, 1925, **25**, 114.

³ *Göttingen Thesis*, 1884.

⁴ *Trans. Path. Soc.*, London, 1879, **31**, 92.

⁵ *Ibid.*, 1857, **8**, 149.

⁶ *International Clinics*, 1925, **4**, 181.

whom the pulmonary artery, small and constricted, arose from a small, thick-walled, left ventricle to the right and anteriorly, while the aorta arose from the same cavity posteriorly, and communicated with the right ventricle through a defect in the septum. *Both vessels may arise transposed from a common ventricle*, as in two examples of cor biatriatum triloculare with pulmonary atresia and transposition, and in the biloculate heart reported by Rudolf. The remarkable cases of displacement of both auricular appendages to the left of the transposed vessels fall in this category. Finally, the transposed vessels may arise from a rudimentary cavity cut off by an anomalous septum from the common ventricle.

The condition of the semilunar cusps in transposition is of interest. In one or other of the vessels, more commonly in the pulmonary, they are frequently deformed, of unequal length, bicuspid, or, as in Bokay's case, markedly increased in depth. Their position varies with the degree of displacement, and should therefore be carefully observed, as the degree of deviation may be thus detected. In true transposition, for instance, the non-coronary cusp in the aorta lies anteriorly instead of posteriorly.

Changes in the relative size and thickness of the two great trunks are usually present, and are of importance as supporting Rokitansky's view that an altered position of the aortic septum is a fundamental part of the condition. In spite of the fact that the pulmonary arises from the left ventricle, which is anatomically constructed as the strongest of the two chambers, this vessel is usually thin-walled and narrowed and its orifice is stenosed or atresic, while the aorta is dilated. Among Rokitansky's 18 cases of transposition, pulmonary stenosis or atresia occurred 11 times, and it was present in 17 out of the 25 cases of Keith's series. In a few instances the reverse holds good and a large thick-walled pulmonary may be combined with a short, narrow aorta. Thérémín's series of 14 cases in infants, 10 of which were of complete and 4 of partial transposition, forms a remarkable exception to the above statement. In 3 of his cases the pulmonary was dilated, and in the remainder it was equal in size to the aorta. In our own series, which includes these 14 of Thérémín's, among 88 cases, in 58 of which the transposition was complete, in 25 partial, and in 5 "corrected," the pulmonary was stenosed or atresic in 28 cases. In 4 cases (Thérémín, 2 cases, Bissell, Robertson), tricuspid atresia was associated, and in 1 (Abbott and Dawson) aortic atresia.

The Fetal Passages.—In complete transposition the venous blood from the right heart is distributed to the arterial system through the aorta, while the aërated blood entering the left auricle is returned again to the lungs by the pulmonary artery. The conditions of the circulation are thus of the poorest, and unless one or other of the fetal passages remains open, life cannot be sustained. The interventricular septum is frequently entire, but a widely patent foramen ovale is nearly always present and combines with a patent ductus or with a septal defect to allow of the passage into the aorta of the aërated blood. Very rarely does one of these conditions exist singly. In our series, among 58 cases of complete transposition the foramen ovale was patent 48 and the ductus arteriosus 39 times. A patent foramen was the only communication

between the two sides of the heart in 7 cases, namely, those by Emanuel, Dorning,¹ Kelly, Cockle, Bokay, and in 2 of Thérémín's cases. It was combined with a patent ductus in 23 cases, with a defect of the inter-ventricular septum in 9, and with patency of both of these openings in 9 cases. The ventricular septum was completely closed in 33 cases and was defective in 26, in 1 of which, that by Heuyer and Campergne,² a localized septal defect was the only communication, and in another by Guttman³ the ductus arteriosus was also patent. In Thérémín's thirty-seventh observation and in Ramm's case, a large patent ductus was the only communication between the right and left heart. In a few cases the bronchial arteries were markedly dilated.

Bokay⁴ made an analysis of 43 cases of complete transposition with regard to the condition of the fetal passages and there are 51 additional cases with fetal passages noted in our series. The table shows the condition of these passages in the combined 94 cases.

No. of cases.		Fetal passages patent.		
		D. A. patent.	A. S. defect or patent F. O.	Defect V. S.
10	Patent, D.A. defect A.S. defect V.S.	10	10	10
45	Patent, D.A. defect A.S.	45	45	..
4	Patent, D.A. defect V.S.	4	..	4
4	Patent, D.A. only communication	4	..	..
10	Defect A.S., and defect V.S.	..	10	10
14	Defect A.S., or patent F.O. only opening	..	14	..
7	Defect V.S., only opening	..	..	7
94	Total patency	63	79	31

The abbreviations are as follows: F. O., foramen ovale; D. A., ductus arteriosus; V. S., interventricular septum.

In other words, all three passages were open in 10 cases; the ductus was patent and a communication existed between the auricles while the ventricular septum was closed in 45 cases; the ductus was patent, and a ventricular septal defect existed but the auricular septum was closed in 4 cases; a patent ductus was the only opening in 4 cases; the ductus was closed, but a communication existed between both auricles and ventricles in 10 cases; a patent foramen ovale was the only communication in 14 cases; and a ventricular septal defect was the only opening in 7 cases, of this combined series of 94 cases of complete transposition. Also, as regards the state of the individual fetal passages the ductus arteriosus was patent in 63 of the cases, the auricular septum was defective or a patent foramen ovale existed in 79, and there was a defect of the inter-ventricular septum in 31.

Hypertrophy and Dilatation of the Heart.—Under the altered conditions the aorta is required to supply blood, not only to the systemic circulation, but through one or other of the persistent fetal passages to the lung. The right heart is practically invariably hypertrophied and dilated, sometimes to an enormous extent, and the right auricle likewise. The left chambers usually share in these changes though to a less degree.

¹ *Trans. Am. Ped. Soc.*, 1891, **2**, 46.

² *Bull. de la Soc. Anat.*, April, 1913, p. 209.

³ *Deutscher med. Wchnschr.*, 1893, **90**, 74.

⁴ *Arch. f. Kinderheilk.*, 1911, **55**, 321.

Symptoms and Physical Signs.—During the period of fetal circulation, transposition of the vessels is of little pathological significance, so that, unless associated anomalies exist, the subjects are born at full term, well developed, and apparently normal. In complete transposition, marked cyanosis is almost always a prominent feature, but it may not be present at birth, appearing usually after some days or weeks, and perhaps developing, as Thérémín suggests, as the ductus becomes obliterated. On account of the extreme degree of the cyanosis, clubbing of the fingers and toes usually develops in infants which have survived the first six months of life. In partial transposition, on the other hand, or in complete transposition with large septal defects, cyanosis may be quite moderate in degree. In Thérémín's patient, dying at three and a half years, there was no cyanosis until the last illness, but large defects of interauricular and interventricular septa combined to relieve the situation. In a remarkable case of partial transposition, recorded by Lebert,¹ death occurred from failing compensation, at the age of twenty, without any sign of cyanosis having developed during life. The patient was a young man in good health until three years previously, when cardiac symptoms developed suddenly after lifting a heavy weight. The aorta arose in front of the pulmonary from the right ventricle, the pulmonary was stenosed and a large septal defect admitted the index finger.

In uncomplicated cases, and where a ventricular septal defect is either not present or is of small size, *physical examination may yield no evidence of the defect*, except a sharply accentuated second sound over the pulmonary (aortic) area. The combination of marked cyanosis with signs of hypertrophy of the right heart and an entire absence of adventitious sounds, or precordial thrill, in an infant or young child, is strongly suggestive of transposition, and a successful diagnosis has frequently been made on these features. In Thérémín's thirtieth observation this was based upon "cyanosis increasing when the infant cried, hypertrophy of the heart both in vertical and transverse diameter, the heart sounds loud and accentuated but pure, the aortic and pulmonary sounds distinct." In Ramm's case, aged fifty-six days, a probable diagnosis was made. Here also there was cyanosis from birth, no murmur, no accentuation or reduplication of the heart sounds, but dulness extending beyond the right sternal border and upward to the second rib, of so marked a character that a mediastinal tumor was at first suspected. In Thérémín's thirtieth, thirty-first, thirty-eight, and thirty-ninth observations the heart sounds were free from murmurs, although muffled, and cardiac dulness was increased to the right. On the other hand, a loud systolic murmur with maximum intensity at the apex was heard in Kelley's case, the same at the base and at the back in Pye-Smith's, and was probably produced by the patent foramen ovale present.

The patent ductus, patent foramen, or septal defect present, may produce their characteristic physical signs, and thus obscure the negative character of the auscultatory phenomena, which is significant of the clinical picture of an uncomplicated complete transposition.

¹ *Virchow's Arch.*, 1863, 82, 405.

Prognosis.—The duration of life varies in the three groups distinguished. In complete transposition it is usually very short and this is especially true of the cases with closed interventricular septum. In 27 of the 33 cases of this type in our series the age at death varied between eleven months and a few days as also in 15 of the 25 cases in which a ventricular septal defect was associated. In the presence of the latter condition life may be considerably prolonged, and the age of sixteen years was attained by Keith's and eleven years by Emmanuel's patient. In cases of complete absence of the ventricular septum, as in the *cor biatriatum triloculare* described by Young, Peacock, Marchand and others, the patients have lived to advanced middle life, and in biloculate heart, such as the cases described by Weiss, Rudolf, and Watton and Abbott, transposition of the great trunks appears to facilitate the circulation, as shown by the comparatively advanced age to which some of these patients lived. On this account the 58 cases of complete transposition here studied have been classified according to the presence or absence of a defect of the interventricular septum. In partial or corrected transposition on the other hand, early adult life is usually reached. Birmingham's patient was twenty, Tonnie's twenty-one, Elliott's¹ nineteen, Young's thirty-six, and Geipel's forty-six years. Vierordt gives an analysis of the duration of life in 75 cases. To this is added that of the 88 in our series, of which there were 62 classified as the primary lesion, and 26 complicating other defects.

CASES IN THIS SERIES.

Age.	Complete.		Partial.	Corrected.	Totals, our series.	Vierordt's cases.
	Closed, V. S.	Defect, V. S.				
Born dead	1	0	0	0	1	3
1 to 24 hours	0	1	0	0	2	1
1 to 7 days	2	1	0	0	4	7
1 to 14 "	6	0	2	0	8	5
14 to 30 "	4	1	2	0	7	7
1 to 2 months	7	2	1	0	10	14
2 to 6 "	7	3	2	2	14	12
6 to 12 "	3	7	1	0	11	9
1 to 2 years	0	2	2	0	4	2
2 to 5 "	2	3	0	0	5	6
5 to 10 "	0	2	2	0	4	0
10 to 11 "	1	0	1	0	2	3
11 to 21 "	0	1	6	1	8	0
21 to 30 "	0	1	1	2	4	5
30 to 40 "	0	1	0	0	1	1
40 to 50 "	0	0	0	0	0	0
Age unmentioned	0	0	2	0	0	0
	33	25	22	5	85	75

PULMONARY STENOSIS AND ATRESIA

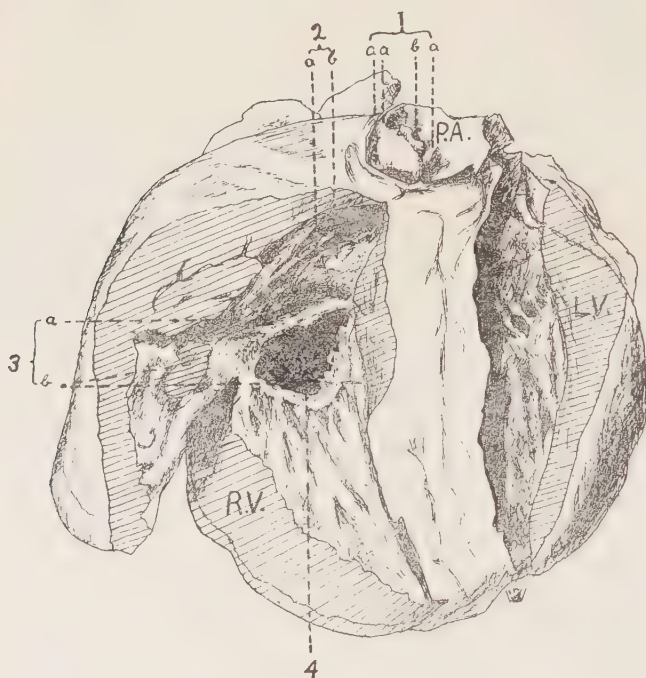
Pulmonary stenosis is the form of cardiac defect most familiar to the practitioner. It is of much clinical importance on account of its comparative frequency, the relatively long duration of life, and the prominence of the cyanosis nearly always associated. To the student also it is a sub-

¹ *Jour. Anat. and Physiol.*, 1877, 11, 302.

ject of the highest interest, for in its symptomatology and pathogenesis are focused the most difficult problems of congenital cardiac disease.

Owing to the wide variations in the conditions presented and the differing aspects from which the subject must be approached, a classification of the different forms is as difficult as it is necessary. Rauchfuss points out that the simple anatomical findings furnish the best guide to

FIG. 75



Pulmonary stenosis of inflammatory origin with fusion of cusps and pinhole orifice surmounted by a row of warty vegetations. Ventricular septum closed. From a girl, aged fourteen years, dyspnoea and cyanosis first noted at the age of nine. Drawing by W. W. Beattie from the specimen in the Pathological Museum of McGill University. Reported by M. E. Abbott, D. S. Lewis and W. W. Beattie, *Am. Jour. Med. Sci.*, 1923, 165, 640.

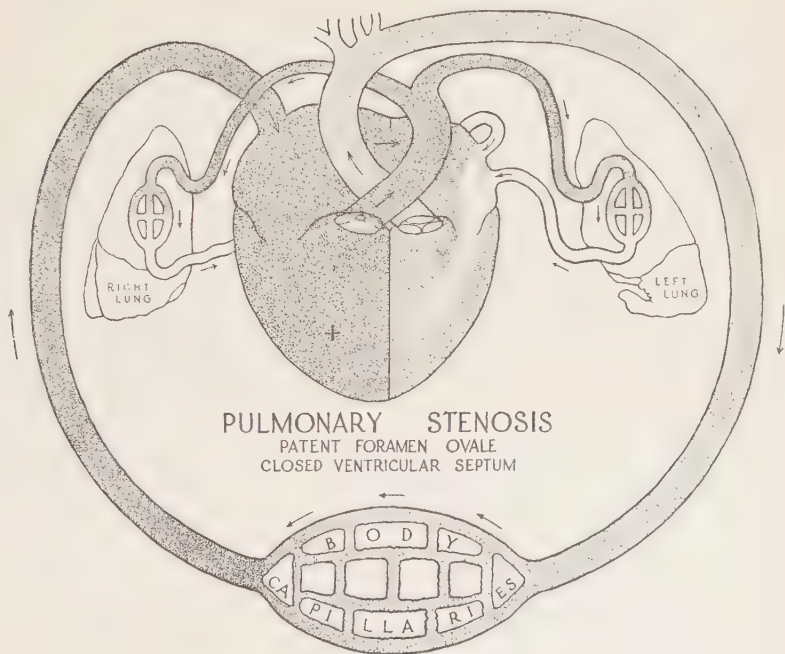
(1) The fused cusps of the pulmonary valve with raphe *a, a, a*, showing the line of attachment to each other; *b*, central pinhole orifice with edges surmounted by a row of vegetations; (2) conus of right ventricle showing; *a*, puckering of musculature; and *b*, a white patch of thickened endocardium; (3) lower bulbar orifice formed by; *a*, crista supra ventricularis; and *b*, trabecula septomarginalis (moderator band); (4) tricuspid orifice, edges of cusps thickened and surmounted by warty vegetations; *A*, aorta, *P.A.*, pulmonary artery; *R.V.*, right ventricle; *L.V.*, left ventricle.

a useful grouping. Thus, the *degree of narrowing* is important, and a simple stenosis is to be distinguished from a complete atresia; from the stand-point of pathogenesis, the *seat and character of the stenosis* are criteria of much value; and thirdly, the *presence or absence of defects of the interventricular septum* provides a dividing line of the greatest importance. This last is important etiologically as indicating the stage of embryonic or fetal life at which the stenosis took place, and clinically

in that the duration of life and symptomatology differ considerably in the two groups.

Statistics.—Pulmonary stenosis is probably the commonest of all cardiac anomalies. The cases are scattered so freely through the literature that an exact statistical statement is impossible. Vierordt estimated at least 300 in 1898, and placed coarctation of the aorta next in frequency with 130 cases. Among 181 anomalies of the heart which he analyzed, Peacock found 119 of pulmonary defect. In 1906 Keith¹ examined 185 specimens of cardiac malformations in the hospital museums of London, and found that in 135, or 70 per cent., there was an anomalous con-

FIG. 76



Venous arterial shunt. Diagram showing the course of the circulation (right to left shunt) in pulmonary stenosis of inflammatory type with closed ventricular septum and patent foramen ovale. (The calibre of the pulmonary artery is not reduced, but the stenosis is *valvular*, the segments being fused, and the lumen narrowed at the pulmonary orifice.) Diagram by W. T. Dawson. By courtesy of *International Clinics*.

dition of the pulmonary tract, the deformity being in the conus of the right ventricle in 133 cases and in the pulmonary valve in 22. In his later communication,² among 272 malformed hearts examined in the various London Museums, Keith found 141 in which the defect was due to an imperfect transformation of the bulbus cordis of the embryo. Of these 141, in 19, there was incomplete fusion of the infundibulum with the body of the right ventricle (conus a separate

¹ *Festschrift, Quatercentenary Aberdeen University*, July, 1906.

² *Hunterian Lectures, Lancet*, 1909, ii, 359, 433, 519.

chamber); in 44, partial arrest in development of the infundibulum; in 37, complete arrest of the infundibulum; in 23 fusion of semilunar valves; in 7, partial or complete absence of the body of the right ventricle with development of the infundibulum; in 4 subaortic stenosis; and in 7, congenital aortic stenosis.

Among the cases of anomalies analyzed here, there are 173 of congenital pulmonary disease. The proportion of stenosis to atresia in recorded cases analyzed is as follows:

	Stenosis.	Atresia.	Number analyzed.
Kussmaul	64	26	90
Rauchfuss	81	33	114
Peacock	90	29	119
Vierordt	83	24	107
Thérémín	20	10	30
This series	130	43	173

The relatively high percentage of atresia in Thérémín's cases is explained by the fact that his material was entirely among infants, in whom the mortality from atresia is high.

The condition of the fetal passages was the subject of statistical study by Meyer, Kussmaul, Taruffi, and other authors, of whose work a full review is given by Vierordt. A defect of the interventricular septum exists in the great majority. The number of cases with closed septum is relatively larger in atresia than in stenosis; thus Rauchfuss finds among 192 cases, 171 in which the interventricular septum is defective and 21 in which it is closed. Of these 21, 10 are cases of atresia and 11 of stenosis. Among Vierordt's 83 cases of stenosis are 71 with defective and 12 with closed interventricular septum; among his 24 of atresia, in 14 the septum was defective and in 10 it was closed. When the interventricular septum is entire, the foramen ovale is usually widely patent, but it also may in rare cases be closed.

Among the 130 cases of stenosis analyzed here the interventricular septum was defective in 105, and entire in 25 cases. In 18 of these 25 the foramen ovale was patent, but in 7 the auricular septum was entirely closed, and no communication existed between the two sides of the heart. Among the 34 cases of atresia the interventricular septum was defective in 24 and entire in 10 cases. Of these 10, in one the foramen ovale was also closed but there was a large patent ductus. The ductus arteriosus is nearly always patent in atresia but is usually closed in stenosis. Among the 96 cases of pulmonary stenosis classed as the primary lesion in the chart, the ductus was patent in only 12; of the 31 cases of atresia, it was patent in 21 cases. The condition of the cardiac septa and ductus in the cases classed as the primary lesion was as follows:

	Stenosis.		Atresia.	
	Number analyzed.	Number with patent D. A.	Number analyzed.	Number with patent D. A.
F. O. and V. S. closed . .	7	0	1	1
F. O. patent, V. S. closed .	16	1	6	5
F. O. closed, defect V. S. .	44	5	10	6
F. O. patent, defect V. S. .	29	6	14	9
Total	96	12	31	21

Rechtslage of the aorta is present in the majority of cases with septal defect, and is especially frequent in atresia. Among the 73 cases of pulmonary stenosis with septal defect, classified in the chart as the primary lesion, it was present in 45 cases, in 33 of which the aorta arose from both ventricles above the defect, and in 12 chiefly or entirely from the right ventricle. Among the 24 cases of atresia with septal defect the aorta arose from both ventricles above the defect in 8, entirely from the right ventricle in 12.

Pathology.—Pulmonary Stenosis.—The narrowing may involve the whole pulmonary tract, or be localized to the valve, artery, or conus. Two distinct types may be recognized:

1. In a few cases the stenosis is valvular in character and is produced by a thickening, shortening, or fusion of the pulmonary cusps. A thick diaphragm with three raphe of fusion on its arterial surface is usually formed, which protrudes into the pulmonary artery in a funnel-shaped way and is perforated by a circular or triangular opening of varying size. The pulmonary artery is frequently dilated above, may be normal, or somewhat thin-walled. The conus below the valve shares in the hypertrophy of the right ventricle, but is otherwise normal; the interventricular septum is usually closed. There is every evidence to show that the stenosis has originated in an inflammatory process in later fetal life after the heart has been fully formed.

2. In the second and larger group, the cusps may or may not be thickened or fused, but the stenosis is due to a rudimentary condition, hypoplasia, or deformity of some part of the pulmonary tract. In these cases a defect of the interventricular septum is usually associated and a deviation to the right of the aorta, so that this arises from both ventricles above the defect, or chiefly from the right ventricle, communicating with the left through the defect. Such forms, which suggest a developmental origin, make up the great majority of cases of pulmonary stenosis, and the combination of these three conditions, pulmonary stenosis, defect of the septum at the base, and *rechtslage* of the aorta, is probably the commonest of all cardiac anomalies.

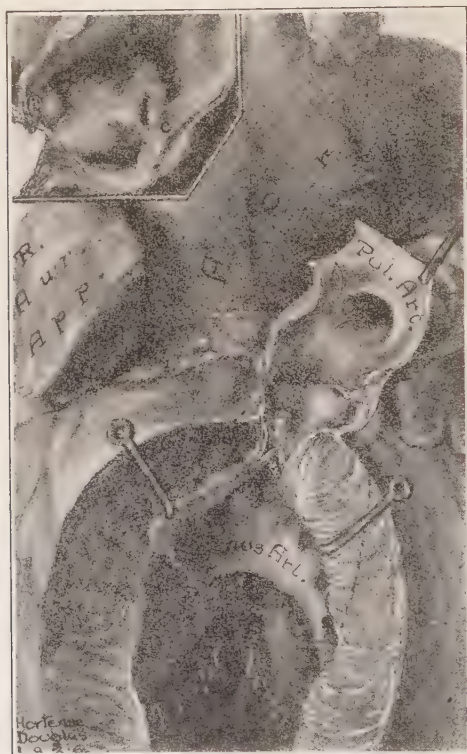
In the majority of cases—in Keith's estimate 90 per cent.—the conus of the right ventricle is involved in the deformity. Two distinct types of conus stenosis may be distinguished. The whole infundibulum may be more or less constricted, its musculature thickened, and the endocardium opaque. In a case of this kind, reported by Cautley,¹ the pulmonary cusps were delicate and healthy above the stenosis, but both they and the artery were very small. Usually the valves are thickened, fused, or rudimentary, and they are often bicuspid. Sometimes a thin diaphragm with delicate raphe showing no sign of inflammatory change, is stretched across the pulmonary orifice, suggesting an incomplete division of the endocardial cushions. In these cases a defect of the septum is almost invariably present.

A second group of conus deformities is that in which a cavity, described by some of the older pathologists as a third ventricle, is cut off from

¹ *Edin. Med. Jour.*, 1902, **12**, 257.

the sinus of the right ventricle by a definite septum perforated by a small opening. There are 19 in this series, including one case of atresia. Keith describes and figures an illustration of this anomaly. The infundibulum is enormously dilated and communicates with the sinus by a small opening with thickened fibrous borders. The pulmonary cusps

FIG. 77



Pulmonary stenosis with defect of the interventricular septum and dextroposition of the aorta. From a case under the care of Dr. C. P. Howard at the Montreal General Hospital. Drawing by Miss Hortense Douglas.

The view is of the interior of the conus of the right ventricle which is greatly narrowed with hypertrophied walls and shows lumen of the pulmonary artery which is hypoplastic and the pulmonary valve of which the cusps are fused into a solid disk with a small asymmetrically placed orifice. In the upper left corner is a detailed drawing of this orifice which shows the raphes of fusion (*a, b, c.*) of the three cusps still evident at their attachment to the pulmonary artery, and the lateral situation of the opening which is drawn over to the right. The greatly dilated aorta is seen above emerging to the right over the septal defect which is hidden by the hypertrophied posterior wall of the conus.

From a man, aged twenty-three years with extreme cyanosis and marked clubbing of the extremities, polycythemia, and epileptiform cerebral attacks.

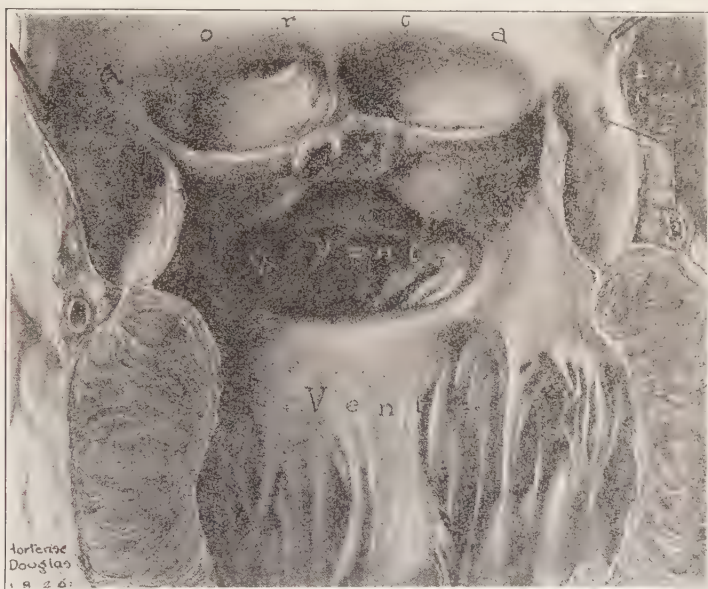
are large and competent, the artery dilated above, and there is a small defect of the interventricular septum. Another variation of this form of conus deformity is figured by Andrewes.¹ The conus is atrophied and is represented by a small cavity with thick muscular walls. It com-

¹ *Trans. Path. Soc.*, 1865, 16, 45.

municates with the sinus of the ventricle by an opening admitting a crow-quill one-quarter inch below the pulmonary cusps, which are small, bicuspid, and not thickened.

Hypertrophy and dilatation of the right ventricle and auricle are constant in pulmonary stenosis, and in the cases associated with defect of the septum at the base and *rechtslage* of the aorta. This latter combination has been given the title "Tetralogy of Fallot," the hypertrophy of the right ventricle constituting the fourth pathological element in this complex. The aorta is usually thick walled and of large calibre. In the developmental cases the pulmonary artery is usually narrow and thin-walled, resembling a vein in structure. When the stenosis is confined to the valve, the artery may be dilated.

FIG. 78



Detail drawing by Miss Hortense Douglas of the heart from Dr. Campbell Howard's case of pulmonary stenosis. View showing the interior of the left ventricle with a large interventricular septal defect just anterior to the pars membranacea and above this the fused right posterior and anterior segments of the aortic valve, which present at the site of their fused corpora Arantii a large ulcerated and calcified area of subacute bacterial inflammation. Note the anomalous chordae tendineae seen through the defect in the right ventricle.

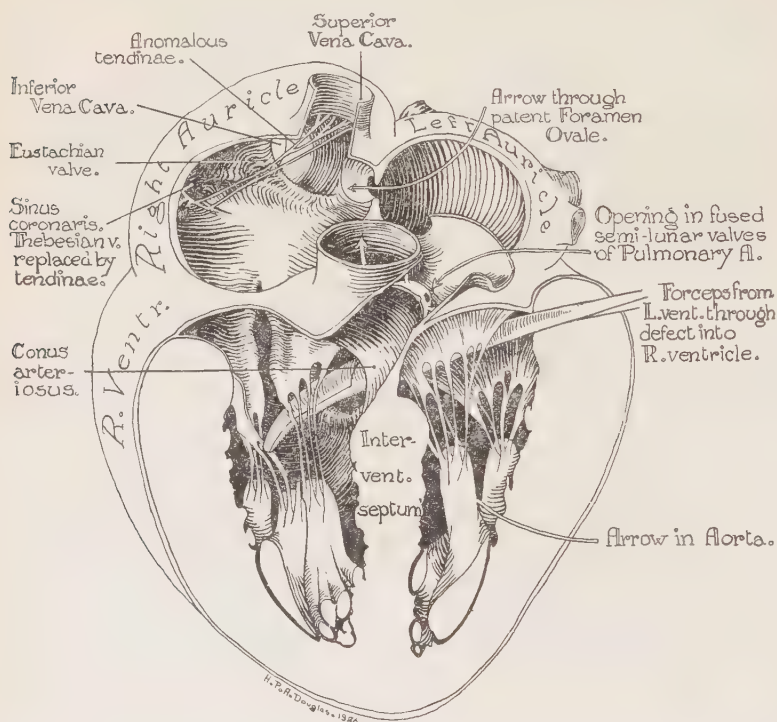
Pulmonary Atresia.—All that has been said of the seat and character of the deformity in pulmonary stenosis applies equally to a complete atresia. In a small series of cases the point of obliteration is at the valve, the artery dilated above, the foramen ovale widely open, and the septum entire. In Weiss¹ case the seat of atresia was in the conus, which admitted only a pinhead or a fine straw, and was lined by thickened endocardium; just above this were two fairly large pulmonary cusps, and the artery

¹ *Brit. Med. Jour.*, 1877, ii, 378.

itself was comparatively large. There was a small patent foramen ovale, a large defect of the septum at the base, and a large thick-walled aorta arose from the right ventricle above the defect.

The pulmonary artery may be obliterated for some distance above the valve, forming a fibrous cord, which may emerge suddenly from the fleshy outer wall of the ventricle and give no sign of its origin from within, or it may be patent throughout, diminishing toward the orifice in a funnel-shaped way. In such cases the cusps may be seen thickened and fused with each other at the bottom of the cul-de-sac formed by the artery,

FIG. 79



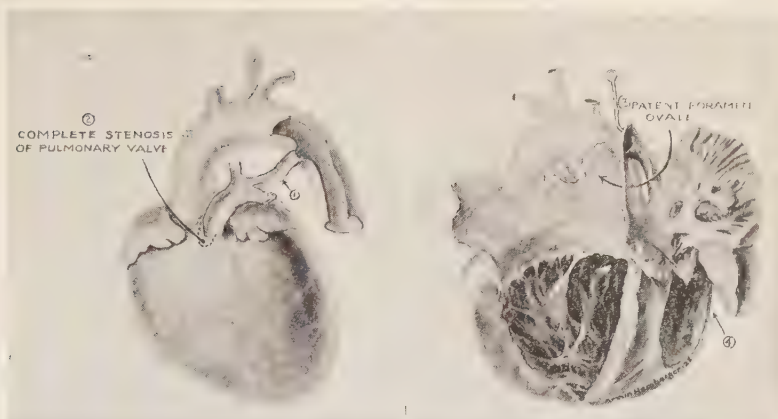
Semi-diagrammatic drawing by Miss Hortense Douglas of Dr. Howard's case of pulmonary stenosis, showing the interior of both ventricles and the relation of the defect to the aortic and pulmonary orifices and the conus arteriosus of the right ventricle.

or they may form a triradiate elevation of three fleshy cushions; or no trace of them may remain. The aorta is usually very large. When a defect in the septum is present it rides over it, or in many cases arises entirely from the right ventricle, as in the case reported by Abbott, Lewis and Beattie.¹

The foramen ovale is frequently widely patent. It may be the only means of communication between the two sides of the heart, the interventricular septum remaining entire. Such cases are less frequent, and

¹ *Am. Jour. Med. Sci.*, 1923, **165**, 636.

FIG. 80

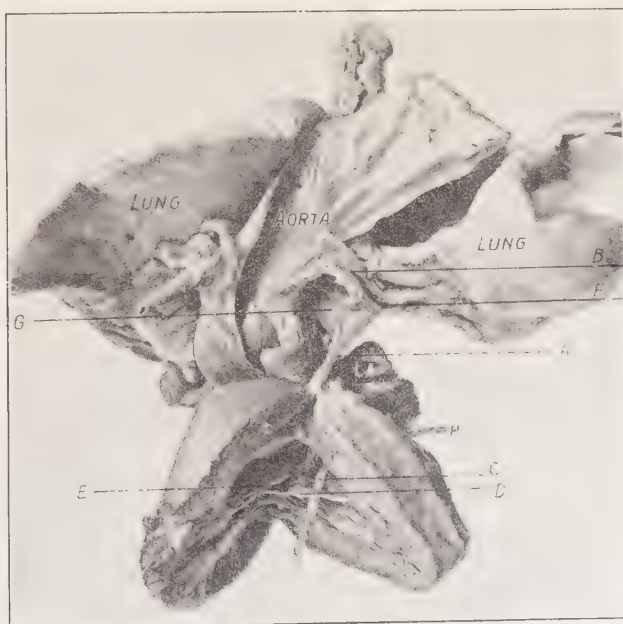


(a) Anterior external view. (1) Patent ductus. (2) Atresia of pulmonary orifice.

(b) View from behind showing interior of left chambers. (3) Patent foramen ovale. (4) Aplastic right ventricle.

Pulmonary atresia and tricuspid stenosis of inflammatory origin. Ventricular septum closed. Ductus arteriosus and foramen ovale widely patent. Right ventricle aplastic. Left chambers dilated and hypertrophied. Right auricle dilated. Case of Dr. Bassen, reported by M. E. Abbott, *Bull. Int. Assn. Med. Museums*, 1924, 10, 111.

FIG. 81



Heart and lungs of an infant, cyanotic from birth, showing: A, atresia of the pulmonary artery; B, patent ductus arteriosus supplying lungs; C, defect of interventricular septum at pars membranacea, guarded by (D) an anomalous valve with false chordae tendineae; E, tricuspid orifice; F, left pulmonary artery; G, right pulmonary artery; H, cord passing through the septal defect; LA, left auricle. (From a specimen in the McGill Pathological Museum, presented by Sir William Osler.)

the condition is more serious in pulmonary atresia than that associated with septal defect.

The alterations in the cavities of the heart vary with the condition of the interventricular septum. When this is entire the left ventricle is greatly hypertrophied and dilated, and both auricles share in the enlargement, while the right ventricle undergoes a true concentric hypertrophy, its wall becoming greatly thickened and its cavity aplasic and lined with opaque thickened endocardium, or in some instances completely obliterated. When a defect of the septum exists, the right ventricle is greatly hypertrophied and is dilated as well, and the right auricle is correspondingly enlarged, the left chambers remaining relatively small. When the aorta rides over the defect in the septum, the left ventricle may share in the hypertrophy.

The Pulmonary Circulation.—When the pulmonary artery is obliterated the blood supply usually reaches the lungs through the widely patent ductus, but this is sometimes closed or absent. Meckel first suggested that in these cases the dilated bronchial arteries might perform this function, and this is usually the case. The lungs were supplied from the left subclavian in Chambers' case, from a dilated ductus arising from the left subclavian in Ramsbotham's. In a case reported by Voss two large bronchial arteries passed into each lung, and were accompanied by an anomalous branch from each coronary. In Koller-Aeby's case the ductus was absent, and three large vessels, equalling the carotid in size, arose from the upper thoracic aorta at the site of origin of the bronchial arteries. The first turned to the right lung, following the bronchi; the others were given off as a common trunk, which divided into a larger branch going to the right and a smaller to the left lung.

Pathogenesis.—Two problems are presented. (1) Is the stenosis of inflammatory or of developmental origin? (2) What is the relation of the septal defect so often associated?

It must be recognized that a small group of cases occurs in which the stenosis is strictly limited to the valves and no septal defect is associated and which present appearances identical with those produced by the chronic valvular disease of postnatal life. Such cases must be supposed to be the result of an endocarditis in later fetal life.

In the large majority of cases a defect of the interventricular septum is associated, indicating that if the stenosis be due to an endocarditis, this must have occurred before the development of the heart was complete at the end of the second month of gestation. It is upon these cases that the discussion really turns. It is evident that if endocarditis can take place during the later stages of gestation, it may occur earlier as well. Campbell and Coulthard found in a patient dying at twenty-eight years, fused pulmonary valves, presenting a central opening admitting a goose quill and surmounted by calcified vegetations. The foramen ovale was widely patent and there was an oval opening 2 x 3 cm. in the lower third of the interventricular septum. The primary condition was a fetal pulmonary endocarditis with resulting stenosis and the ventricular defect was a secondary arrest of development for the better carrying on of the circulation. On the other hand, there are many cases in which the

presence of associated defects and the absence of inflammatory action show positively that a primary arrest of development has been the cause. This is especially true of pulmonary stenosis of developmental origin associated with dextroposition of the aorta and hypoplasia of the pulmonary tract. In the valvular stenoses and atresias, especially the latter, myocardial disease, probably of syphilitic origin and acting by obliteration of the conus below the valves, is frequently the causative factor.

Reference has been made to the explanation communicated by Keith, which is now generally accepted, that in the majority of cases the stenosis is primary in the conus, and is the result of an arrest of development at a stage when there existed in the heart a fourth primitive chamber, the bulbus cordis. In accordance with the researches of Greil, he describes three changes as taking place in the evolution of the mammalian from the primitive heart of the fish and reptilia: (1) The division of the primitive auricle and ventricle; (2) the submerging of the sinus venosus in the musculature of the right auricle; and (3) the separation of the bulbus cordis from the left ventricle and aorta, and its complete incorporation in the right ventricle as the infundibulum of that chamber. This last change takes place by an upgrowth of the ventricular musculature around the cavity of the bulbus, the musculature of the latter being replaced by that of the ventricle, in the same way as the musculature of the auricle replaces a great part of that of the sinus venosus. The author considers that "*the submergence of the bulbus constitutes a critical phase in the developmental metamorphosis of the heart, and it is during this time that malformations are apt to occur.*"

Four different types of conus stenosis are to be distinguished, of which the first is that well-differentiated form in which the conus forms a separate chamber, being separated from the sinus by a muscular partition. Peacock, in describing a similar case, compared it to the three-ventricled heart of the turtle, and considered that it represented an arrest of development. Keith explains the condition as being simply an arrest of development in which the infundibulum and body of the right ventricle have developed to a normal extent, while a constriction has remained between them, *representing a persistence of the lower bulbar orifice*. The other forms of conus stenosis, in which there is a constriction more or less complete of the whole infundibulum, are evidently the result of an arrest of development of the bulbus as a whole, its musculature failing to become submerged in that of the right ventricle proper.

Pathological Physiology.—Pulmonary stenosis and atresia with auricular or ventricular septal defect, and with or without dextroposition of the aorta, supply the best example of the immediate and remote effects of a high degree of oxygen-unsaturation persisting throughout many years, and illustrate the combined effect of a permanent venous-arterial shunt of the circulation through the septal communication as a result of the raised pressure in the right ventricle, and of an increased deoxygenation in the systemic capillaries from retardation of flow there. In no other condition of congenital cyanosis does such an extraordinary degree of clubbing and cyanosis retinæ, viscosity of the blood and polycythemia become evident as in many of these patients who have reached

maturity. Wherever a free septal communication is combined with pulmonary hypoplasia or stenosis, whether in the valves or conus or both, and the condition has lasted into adult life, the symptom-complex of congenital cyanosis is markedly seen. In pulmonary atresia life is shorter, so that while cyanosis is prone to be more intense, the remote effects of the raised oxygen-unsaturation usually have not an opportunity of developing so completely; in the few cases of pulmonary atresia with widely open ventricular septum and aorta rising entirely from the right ventricle when the patients live longer (eleven to thirteen years), the clinical picture closely resembles that of pulmonary septal defect and dextroposition of the aorta (Fallot's Tetralogy).

In a few rare cases of pulmonary stenosis the cardiac septa and ductus arteriosus are all closed, and no communication appears to exist between the pulmonary and systemic circulations. This was the condition in 2 cases described by Peacock,¹ and in 1 by Ogle. In one of Peacock's cases cyanosis was "slight" and in the other 2 entirely absent, although they reached the ages of twenty-three and fourteen years. This suggests that the main cause of the cyanosis in pulmonary stenosis is the venous-arterial shunt through an associated defect, and not the retardation of flow in the capillaries.

Paradoxical Embolism.—Owing to the raised pressure in the right chambers, in the presence of an associated interauricular or interventricular septal defect, the conditions for the occurrence of a crossed embolism from thrombi lodged within the right cavities or auricular appendix, or for the passage of fragments from thrombosis in the systemic veins, are extremely favorable, and it is not uncommon to find infarcts in both circulations indicating that this has occurred. Dextroposition of the aorta with associated ventricular septal defect makes the mechanical conditions still more favorable for the passage of such an embolus. The cerebral abscess so common in congenital cases of this type following operative procedures, appears to be undoubtedly due to an infective embolus of paradoxical origin. In our series of 96 cases of pulmonary stenosis, paradoxical embolism occurred 6 times; and among the 31 cases of pulmonary atresia it occurred once. In 6 of these 7 cases the embolism was to the brain, resulting in a cerebral abscess, and in 1 case it was into the femoral artery.

Associated Anomalies.—These were usually absent in the cases of pulmonary stenosis with closed septum, a fact arguing for an inflammatory origin of the stenosis during fetal life after the septa were closed. In our series of 23 cases with closed septum there were only 3 with associated anomalies and these were minor conditions, coarctation of the aorta (Lafitte), double left coronary (Abbott, Lewis and Beattie), and asymmetry of the calcarium (Beck). In the cases of pulmonary stenosis with septal defect and in pulmonary atresia grave cardiac defects or anomalies elsewhere in the body are usually present and argue in favor of the developmental origin of the majority of these cases. Among the 73 cases of pulmonary stenosis with defect of the ventricular septum

¹ *Trans. Path. Soc.*, London, 1859, 10, 122; 1878, 30, 258.

classed as the primary lesion in our series, associated anomalies in the heart or great vessels were present in 34 cases and anomalies elsewhere in the body in 8. Coarctation of the aorta occurred in 5 cases, right aortic arch in 2, anomalous origin of the ductus (*a*) from the innominate artery and (*b*) from the concavity of the arch by a double opening (2 cases), anomalous network in the right auricle in 1, persistent left superior cava in 1, abnormally large Eustachian valve in 2, bicuspid aortic valve in 3 cases. A huge nævus occupying one side of the face, absence of the left kidney, absence of the spleen, idiocy and asymmetry of the calvarium with great thickening of the cranial vault have been reported. In Ettlinger's case there was a large defect in the interauricular septum above, with multiple defects of the interventricular septum, and the pulmonary veins opened into the right auricle. In Habershon's there was false dextrocardia, tricuspid stenosis, defect of the interventricular septum, and horseshoe kidney.

A fact of much importance is the presence of associated anomalies in cases of atresia with *closed* ventricular septum, which might reasonably be considered to be of inflammatory origin. It seems probable that the primary condition here was a narrowing of the conus or orifice in an arrest of development, and that the obliteration was produced by an active myocarditis supervening in later fetal life.

Symptoms.—The majority of cases of pulmonary stenosis and all cases of pulmonary atresia present the classical picture of congenital cyanosis in all its details. So frequent is the association between the two conditions, that *morbus cœruleus* and pulmonary stenosis have been considered almost synonymous terms. The clinical aspects vary to a certain extent with the presence or absence of defects of the interventricular septum, and with the degree of deformity. In stenosis with closed ventricular septum cyanosis is usually slighter and of later incidence, and the duration of life much longer; in a few rare instances with closed septa cyanosis has been absent throughout life. The most typical instances of congenital cyanosis with bluish discoloration of the skin, becoming pronounced on exertion, clubbing of the fingers, dyspnoea, and cyanotic attacks are seen in the many cases in which pulmonary stenosis is combined with defect of the septum and *rechtslage* of the aorta. Pulmonary atresia differs from a simple stenosis in the still more extreme degree of the cyanosis. These are the cases of true *morbus cœruleus*, in which a constant deep blue, or even purple, discoloration exists, increasing to black on violent exertion. Here the opposite condition in relation to septal defects is seen. When the septum is closed the cyanosis is more extreme and the duration of life correspondingly shorter.

Physical Signs in Pulmonary Stenosis.—These are generally distinctive, but may be obscured by those of the septal defect so often associated. In typical cases, enlargement of cardiac dulness to the right and above, precordial bulging, epigastric and precordial pulsation indicate an enlargement of the right heart. Sometimes the cardiac impulse may be so violent that the head and neck share in the vibration of the chest. A thrill, localized to the second and third left spaces, or diffuse over the precordium, is fairly frequent. Its presence seems to depend somewhat

upon the condition of the septa. Rolleston,¹ in reporting a case of stenosis with *rechtslage*, in which there was no precordial thrill, explains this by the presence of a large defect of the septum, through which the blood current passed with ease into the aorta. He says that the evidence in recorded cases is contradictory upon this point, and suggests a statistical study of it. A thrill was present in 23 of the 96 "primary" cases analyzed. In these the condition of the fetal passages was as follows:

Cardiac septa.	Number of cases analyzed.	Number with thrill.
F. O. and V. S. closed	7	3
F. O. patent and V. S. closed	16	8
F. O. patent, defect V. S.	29	8
F. O. closed, defect V. S.	44	4

That is to say, in more than one-half of the cases with closed ventricular septum a thrill was present, as also in 8 of the 29 in which both foramen ovale and ventricular septum were open. But in the 44 cases with closed foramen ovale and with defect of the septum a thrill was absent in all but 4; in one of which there was a large patent duct, which was apparently the cause.

These figures are puzzling at first, but interesting on reflection, and are large enough to be of value as facts. The inference is that a thrill is frequently present when the interventricular septum is entire, and also when a defect of that septum coexists with a widely patent foramen ovale; when the interauricular septum is closed and the interventricular open a thrill is rare, and when it does occur may perhaps be ascribed to the associated septal defect. Further statistics are needed.

The pulmonary second sound is weak or absent in a certain proportion of cases. Much stress has been laid upon the absence of pulmonary accentuation as a diagnostic sign of pulmonary stenosis, but in a limited number of the cases it has been distinctly louder than normal.

A prolonged, harsh, rasping, or blowing systolic murmur heard over the whole cardia, but chiefly at the base, with its point of maximum intensity to the left of or over the upper part of the sternum and the second interspace, is present in the great majority. It is transmitted upward toward the clavicle, along the course of the pulmonary artery, and over the sternum, but is faint or inaudible at the apex and to the right of the sternum. It may be so loud as to be heard over the whole chest. From this type important variations occur. (1) The murmur may be heard over the whole cardia, but with maximum intensity at the apex, as in Cassel's case, a boy aged thirteen years, with pulmonary stenosis and a patent foramen ovale, but the ventricular septum entire. (2) In cases in which the septal defect is present the murmur may be heard over the aortic area and *along the carotids*. Eisenmenger mentions this as a diagnostic point for the association of pulmonary stenosis with a septal defect. In Scheele's² case, a girl aged fifteen years, with marked cyanosis, the pulmonary orifice admitted a thin pencil, the valves were small and shrunken, the conus was reduced to the size of a pea, and the septum

¹ *Trans. Path. Soc.*, London, 1892, **43**, 32.

² *Deutsches med. Wchnschr.*, 1888, **40**, 294.

was defective at the base. There was a systolic murmur along the course of the pulmonary artery and at the left sternoclavicular articulation, which was transmitted far up the carotids and along both subclavians, and was most marked over the left carotid. It was heard also at the aortic cartilage. (3) The murmur may be heard in the back, in the left infra-scapular region. This occurred in a number of the cases in this series, but in all a septal defect was associated, to which the transmitted murmur was probably due. (4) In a few cases physical signs are absent. Variot reports a child aged five years, with a large defect of the septum, and the pulmonary a small thin cord with rudimentary valves, who presented marked cyanosis with clubbing, but whose heart sounds were clear.

Roentgen-ray, Electrocardiographic, and Blood-gas Findings.—The most characteristic roentgen-ray features are the relatively small size of the left ventricle and the great hypertrophy of the right ventricle, which frequently curves around the smaller left chamber from below, rising upward like the tip of a sabot (Vaquez and Bordet), and giving rise to the descriptive term "*cœur en sabot*," which is characteristic of the more pronounced cases associated with ventricular septal defect and dextroposition of the aorta. There is prominence of the second left or pulmonary arc which is enlarged and pulsating in most cases of pulmonary stenosis of long standing and which has been ascribed, by the French writers especially, to a dilatation of the pulmonary artery above the point of stenosis. Such a dilatation, however, is by no means constant, for, on the contrary, a hypoplasia of the pulmonary artery is associated in most of the cases of stenosis of the developmental type, so that some other causes for the second left arc must be found. Usomoto¹ investigated 10 such cases, in 2 of which autopsy revealed that the large second left arc of the radiograph was due not to a dilated pulmonary artery but to a greatly hypertrophied *conus of the right ventricle*, which underlay the roentgen-ray shadow.

The electrocardiographic tracing reveals right ventricular preponderance much in excess of that shown in any acquired lesion such as mitral stenosis; and an enlarged *P*-wave in the second lead indicative of the auricular hypertrophy and dilatation invariably present in the right auricle.

The high degree of oxygen-unsaturation in the blood can be ascertained by direct analysis and the amount of the venous shunt calculated.

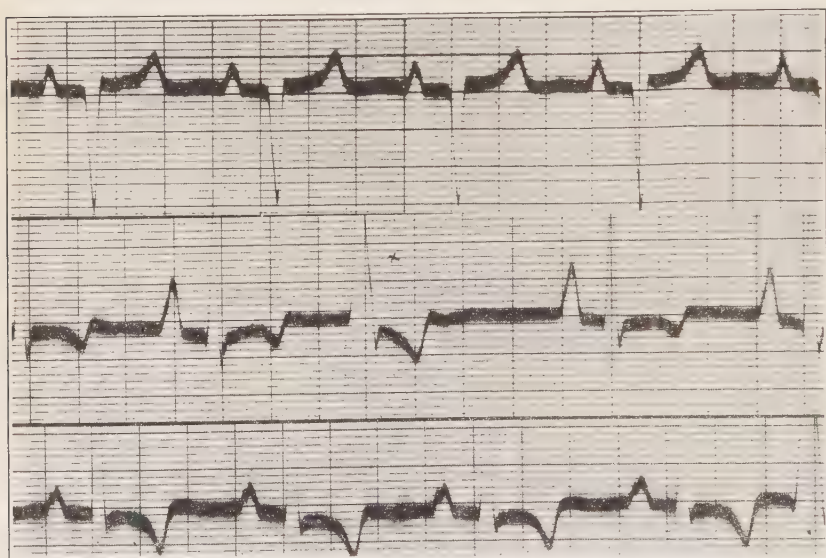
Diagnosis.—In the majority of cases the decided localization of murmur and thrill, the increased cardiac dullness to the right, the absence of pulmonary accentuation, and the presence of the distinctive symptoms of pronounced congenital cyanosis make a positive diagnosis possible. On the other hand, the variation in the character of the murmur and of the pulmonary second sound, and the occasional absence of cyanosis, render the diagnosis indefinite in a certain proportion of cases. That such atypical cases occur also makes it very difficult to exclude the possibility of pulmonary stenosis in the differential diagnosis of other cardiac defects. The presence of constant and marked cyanosis, the distinctive character

¹ *Deutsches Arch. f. klin. Med.*, 1925, **147**, 159.

of the murmur, and the fact that it is not usually heard in the back, are points in favor of stenosis. In patency of the duct, pulmonary accentuation is the rule, in pulmonary stenosis it is the exception.

Both the associated defect in the interventricular septum and the pulmonary stenosis have frequently been diagnosed. The presence of a thrill speaks rather for a closed septum, or for cases in which the foramen ovale also is patent. In a large number of cases the presence of the two distinctive murmurs can be traced, that due to the pulmonary obstruction heard best at the base and transmitted beneath the clavicle, that due to the defect localized at the fourth space, heard also in the back, both harsh, but of the two, the pulmonary usually of a more blowing character.

FIG. 82



Electrocardiogram from Dr. C. P. Howard's case of pulmonary stenosis with defect of the interventricular septum and dextroposition of the aorta, showing right ventricular preponderance, high *P*-wave, and ventricular extrasystole.

Course.—The duration of life in pulmonary stenosis with closed interventricular septum is relatively high. Hebb's patient died at forty-five years, and Lallemand's patient with pulmonary valves fused to form a diaphragm, with a small central perforation in the patent foramen ovale, died at the advanced age of fifty-seven. The lowest age in our series with closed septum was six years. The possibility exists in such cases that the stenosis had advanced, or even originated since birth. In pulmonary stenosis with septal defect death occurs earlier, usually in the first or early in the second decade, but adult life is sometimes attained. The maximum age of the cases with septal defect in this series was thirty-six years (Lafitte), but 28 of the patients died in the first decade and 16 in the second. In pulmonary atresia life is very short. The patients with closed septum all die within the first few months. When a defect of the

interventricular septum exists these subjects may live some years. The highest age recorded was thirteen years, in one of Peacock's cases. The table gives the duration of life in the cases classed as the primary lesion in this series in which this point is mentioned:

PULMONARY STENOSIS.

Age at death.	V. S. closed.	F. O. closed, defect V. S.	F. O. patent, defect V. S.
Within first year	0	4	1
1 to 2 years	0	2	4
2 to 5 years	1	8	3
5 to 10 years	1	12	6
10 to 15 years	6	2	5
15 to 20 years	4	5	4
20 to 25 years	9	7	4
25 to 30 years	0	2	2
30 to 35 years	0	0	0
35 to 40 years	0	1	0
40 to 50 years	1	0	0
50 to 60 years	1	0	0
Age unmentioned	0	1	0
Number of cases analyzed	23	44	29

PULMONARY ATRESIA.

Age at death.	V. S. closed.	F. O. closed, defect V. S.	F. O. patent, defect V. S.
In first week	1	0	0
1 to 4 weeks	2	0	3
1 to 3 months	1	1	2
3 to 6 months	3	2	1
6 to 9 months	0	0	1
9 to 12 months	0	1	5
1 to 5 years	0	3	0
5 to 10 years	0	1	1
10 to 13 years	0	2	1
Number of cases analyzed	7	10	14

The following table summarizes the facts contained in the foregoing tables and contrasts the effects of an interventricular septal defect in *pulmonary stenosis*, in which the *duration of life* is shortened, owing to the increased venous arterial shunt, with those of the presence of a ventricular septal defect in *pulmonary atresia*, in which case the freer circulation permitted enables life to be sustained for some years, instead of terminating, as in the cases of closed septum, in the first weeks or months of life.

Nature of lesion.	Number of cases.	Moderate or marked cyanosis.	Maximum age.	Average duration of life.	Precordial thrill.
<i>Pulmonary stenosis: 96</i>					
(a) With closed septum	23	In 9 (39.5%)	57 yrs.	20.6 yrs.	In 11
(b) With ventricular septal defect	73	In 56 (76.7%)	28 yrs.	10.8 yrs.	In 12
<i>Pulmonary atresia: 31</i>					
(a) With closed septum	7	Extreme in all	6 mos.	12 wks.	In 0
(b) With ventricular septal defect	24	In 22	13 yrs	3.4 yrs.	In 2

Many patients who survive until early adult life die, not of the lesion, but of pulmonary tuberculosis. The cause of this seems to be: (1) The reduced blood supply to the lungs produces an anemic condition which favors infection; (2) the marked cyanosis usually present depresses the general powers of resistance; (3) the subjects of pulmonary stenosis frequently live to an age when tuberculosis is likely to invade the organism when the nutrition is low. This last point is illustrated in an interesting way in this series. Among the 23 patients with closed septum in whom the duration of life was longer, pulmonary tuberculosis occurred eight times (34.7 per cent.). Among the other 73 patients with defect of the interventricular septum (in whom life was shorter) it occurred in 14 cases; all of whom with one exception had passed the age of puberty (14.6 per cent.). Tuberculosis was not present in any of the cases of pulmonary atresia in this series.

The very frequent termination by an infective endocarditis, developing about the margins of the defect or on the wall opposite to it, or in the valves adjacent, has been stressed. It was present in 8 of the 23 cases with closed septum and in 18 of the 73 cases with ventricular septal defect classed as the primary lesion and this incidence would be much higher if one excluded all the cases dying under four years of age, in whom a bacterial endocarditis was not manifest in our series, nor was it present in one of the 31 cases of pulmonary atresia, all of whom died early.

Robinson reports two instances in patients who both died at the age of twenty years, in both of whom the conus formed a separate chamber with narrow bulbar orifice. In the one case there were large vegetations on the conus wall, in the other these formed a fine fringe around its ventricular orifice, and coarse outgrowths about the associated defect in the interventricular septum. Acute endocarditis appears to be especially common in this form of conus deformity, and among the 19 cases in which the conus formed a separate chamber, recent vegetations fringing the conus orifice, on the wall, or on the tricuspid valve were present in 6 instances.

DILATATION OF THE PULMONARY ARTERY AND INSUFFICIENCY OF THE PULMONARY CUSPS

Dilatation of the pulmonary artery is very common in combination with certain cardiac anomalies but is rare as an isolated condition. A few cases are recorded in which it appears to be primary and to originate in an irregular division of the common arterial trunk. The main vessel is diffusely enlarged and its branches are tortuous and dilated, but the heart and lungs are otherwise normal. The artery is usually dilated in persistence of the fetal passages connecting the two sides of the heart, especially in patent ductus and defects of the lower part of the interauricular septum, or in widely patent foramen ovale. In the two latter conditions hypoplasia of the aorta is frequently associated and it is difficult to say which is the primary condition. The dilated artery may be atheromatous even in young subjects. The clinical manifestations of

pulmonary dilatation are discussed by Abrahams¹ with the report of a case in which this was diagnosed as the primary condition.

Pulmonary insufficiency resulting from the destruction of what was thought to be a congenitally stenosed pulmonary valve by warty vegetations of a malignant endocarditis is reported by Cautley in a girl aged fifteen years who had been blue and cold from infancy, with marked thrill and murmur over the pulmonary artery. During the last two and a half years of life the systolic murmur was replaced by a large loud diastolic one with maximum intensity at the third and fourth left interspace and a marked precordial thrill along the left sternal border. The lungs were extremely congested, with multiple infarcts, and hemoptysis occurred during the last weeks of life.

CONGENITAL AORTIC STENOSIS OR ATRESIA

Subaortic Stenosis.—This term has been applied to a curious annular thickening of the endocardium of the left ventricle, a few millimeters below the aortic valves, which involves the base of the aortic segment of the mitral valve, and encircles the ventricular wall at this point, and leads in most of the cases, to a localized narrowing of the cavity. The cases recorded are not numerous, but the condition, when present, usually leads to serious results, and is therefore important. The thickened ring of tissue is often the seat of a chronic inflammatory process, probably of later incidence, but there can be little doubt that it is, at least in a certain proportion of cases, of congenital origin. Microscopic examination of the ring in a case reported by Moore showed it to be non-inflammatory in character. Keith explains it as an arrest of development, analogous to the conus stenosis of the right ventricle, the bulbus failing to atrophy about the root of the aorta.

Endocarditis frequently develops both at the defect and at the aortic valves above it, and may lead to further contraction at these points. Shennan² and Smart³ report 2 such cases under the term "double aortic stenosis," and 1 is recorded by Thursfield and Scott,⁴ in which the aortic orifice was narrowed by a fibrous ring, situated on the interventricular septum, just below the undefended space and extending over the anterior mitral segment, and the aortic valves were thickened and fused; there was a thin line of fibrosis in the otherwise healthy aorta just above the margin of the valves, and slight coarctation at the isthmus. In Shennan's patient, and in that of Fletcher and Beattie, a thick calcareous ring lay below the thickened and ulcerated valves which were the seat of a malignant endocarditis.

Most of these patients reach adult life, and the clinical significance of the condition lies chiefly in the frequent incidence of acute endocarditis, for the fibrous ring or shelf lining the wider aortic conus does not necessarily interfere to any serious extent with the passage of blood into the aorta. Therefore the clinical picture differs from that of a valvular

¹ *Jour. Am. Med. Assn.*, 1913, **60**, 1150.

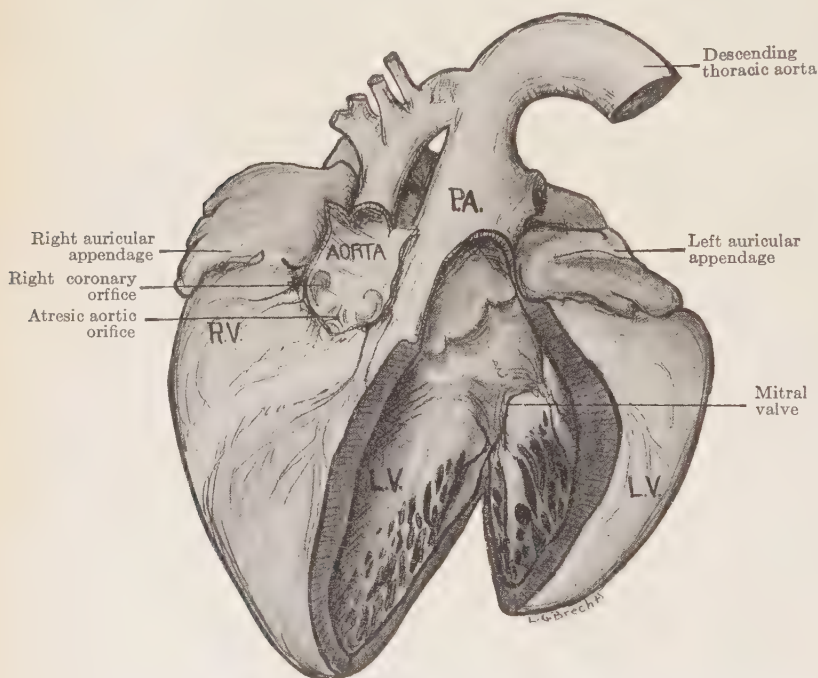
² *Lancet*, 1905, vol. i, 21.

⁴ *Brit. Jour. Child. Dis.*, 1913, **10**, 104.

³ *Ibid.*, 1904, vol. ii, 1417

stenosis at the aortic orifice by the absence of the usual symptoms of a diminished circulatory output, in the presence of a highly characteristic long drawn out harsh systolic murmur with maximum intensity at the third right interspace, but transmitted widely over the whole chest and into the vessels of the neck and accompanied in most cases by a systolic thrill. In one case only of those reported, that by Bret et Blanc Perducat,¹ in a man, aged fifty-eight years, in whom the conus was narrowed a short

FIG. 83



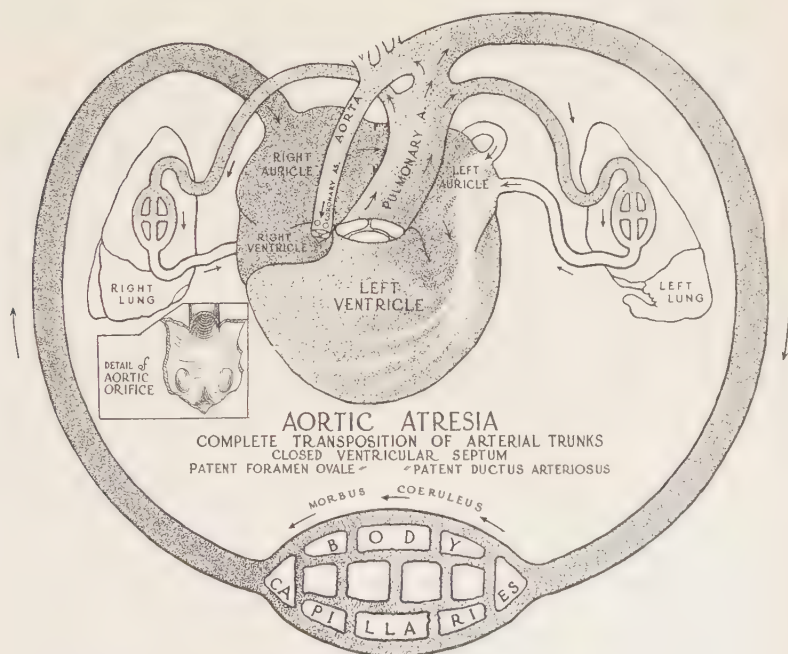
Aortic atresia with complete transposition of great trunks, aorta from right ventricle, to right and anteriorly, pulmonary artery from left ventricle to left and posteriorly. Foramen ovale widely patent, ventricular septum entire. Obliteration of aortic orifice below cusps, dilated pulmonary artery forms descending aorta through widely patent ductus arteriosus. Aplasia of right ventricle and tricuspid orifice, hypertrophy of both auricles and left ventricle. (From an infant dying on seventh day, with difficulty in breathing two days previously. Some cyanosis at the last.) (M. E. Abbott and W. T. Dawson, *International Clinics*, 1924, 4, 2. Published by permission of J. B. Lippincott Company.) Drawing by L. Brecht from the specimen in the Museum of the Woman's Medical College of Pennsylvania.

distance below the aortic valve by a double calcareous ring this prolonged murmur was *diastolic* with a short systolic murmur at the apex. The subjects are commonly strong vigorous young adults who have shown no pallor nor tendency to fainting nor the slow small pulse significant of an aortic obstruction, and who come under observation accidentally, or with the infective endocarditis that is so liable to supervene, and the contrast

¹ *Lyon Méd.*, August 18, 1912.

between this history and physical condition and the extraordinarily loud murmur is pathognomonic. In Goldweizer's¹ patient, aged twenty-one years, with previous history of vigorous health, the heart was enlarged, the apex in the sixth interspace, and a systolic thrill was detected in the third right interspace, and an extraordinarily strong rumbling systolic murmur was heard all over the chest both back and front transmitted into both axillæ and the vessels of the neck, but with maximum intensity at the third right interspace. Death resulted from a pneumococcus endocarditis of the aortic valve; and at autopsy a solid white callous ring encircled the lumen of the aortic conus, being separated from the aortic

FIG. 84



Venous-arterial shunt. Diagram by W. T. Dawson, *International Clinics*, 1924, vol. 4. By permission of Lippincott Company.

valves above it by 1 cm. of healthy endocardial tissue. Goldweizer refers to 20 other cases in the literature and there are 6 in our series which do not appear to be included, making 26 cases on record. Two groups are to be differentiated, (a) those in which the lesion is associated with other anomalies, in which case a true arrest of development with survival of the bulbus cordis in the aortic vestibule has probably occurred (Keith), and (b) a subaortic stenosis of inflammatory origin due to an infective process setting in early postnatal or late prenatal life.

Congenital Stenosis and Atresia of the Aortic Orifice.—Aortic stenosis of antenatal origin is not common and the duration of life with it is

¹ *Mcd. Obor., Mosk.*, 1912, 76, 319.

very short. Two forms may be distinguished; those apparently inflammatory, with the stenosis limited to the valves and the ventricular septum entire, and those apparently due to an arrest in development. Unlike pulmonary stenosis, the inflammatory forms are here the commoner, both those due to fetal endocarditis, with fusion of the cusps, and those in which the myocardium is diseased and the conus narrowed and obliterated directly below the orifice. In extreme cases of aortic stenosis, and in aortic atresia, the left ventricle is aplasic with greatly thickened walls presenting a true eccentric hypertrophy, while the right ventricle is so greatly hypertrophied and dilated as to encircle the left at its apex, forming a recess-like cavity below the latter, and the pulmonary artery, which is much enlarged, forms the descending aorta through the dilated ductus arteriosus. The extreme hypoplasia of the aorta in the cases of congenital aortic stenosis who survive to adult life, commonly leads to a condition known as "aortic dwarfism."

Thérémín collected 17 cases, in only 2 of which was there a defect of the septum. In our series there are 10 cases of aortic stenosis and in only 1 a septal defect; and 6 of aortic atresia with associated septal defect in 5. The foramen ovale and ductus, are nearly always widely patent, the latter supplying the systemic circulation.

Cyanosis is absent in cases of congenital aortic stenosis, but is marked in atresia. Physical signs may be absent, or there may be a loud systolic or double murmur heard over the whole chest. In both conditions the duration of life is very short. In aortic atresia the highest age attained in the 7 cases of our series was sixteen weeks. This was in a case described by Simmon¹ in an infant, cyanotic from birth, with widely patent foramen ovale and ductus arteriosus, the left ventricle aplasic, the right ventricle greatly hypertrophied, and the aortic cusps fused to form a cone.

Left-sided Conus Stenosis.—Schmincke² describes 2 cases in adults of a peculiar muscular stenosis of the conus of the left ventricle, with healthy aortic valves, and no apparent cause, which he thought must be of congenital origin, due to a primary asymmetry in the formation of the left ventricle.

ANOMALIES OF THE SEMILUNAR CUSPS

These cusps may be increased or diminished in number and defective, fenestrated, or otherwise malformed. A row of supplementary cusps may exist or they may be the seat of attachment of anomalous bands.

Increase in Number.—Supernumerary cusps sometimes occur in the pulmonary artery and, less frequently in the aorta. A more or less perfectly formed fourth cusp of varying size, but usually smaller than normal, may be inserted between two of the others. Or the usual number of segments may exist, and the sinus behind one of these be divided by a raphé which runs from the back of the cusp to the aorta, indicating fusion of the additional segment or imperfect division from its fellows. In rare instances five cusps occur. Peacock figures a case of five aortic

¹ *Intercol. Jour. of Austral.*, February 20, 1906.

² *Deutsches med. Wchnschr.*, 1907, 33, 2082.

cusps, and Dilg enumerates from the literature 4 cases, in 2 of which the five cusps were in the aorta, and in 2 in the pulmonary artery.

The subject of numerical alteration of the semilunar cusps was first studied by Osler¹ (1880), who reported 7 cases of bicuspid aortic valve which he believed to be of congenital origin, in one of which the pulmonary valve was also bicuspid, by Dilg² (1883) who reported a case of bicuspid aortic valve complicating subaortic stenosis and added a statistical study of 112 cases from the literature; and by Martinotti and Sperino,³ the latter in a valuable article which describes and figures 7 cases, illustrating various types of increase or diminution of the aortic and pulmonary cusps (3 bicuspid aortic, 1 bicuspid pulmonary, 3 supernumerary pulmonary cusps). Martinotti⁴ later assembled 47 cases additional to the 112 collected by Dilg.

The supernumerary cusps have sometimes been explained as an effort at repair of some inflammatory process of long standing, but when the fourth segment is perfectly formed, or the raphé indicating it shows no sign of thickening (as in a case in the McGill Museum), a true malformation must be concluded, which is usually explained as a formation by excess. As this condition is of congenital origin, the cusps are generally so adapted to each other as to be competent to close the orifice, no insufficiency resulting; they occur usually in a heart free from other malformations, and are of infrequent occurrence. Their clinical significance lies chiefly in their tendency, like all valvular anomalies, to become the seat of endocarditis.

Diminution in Number.—A *bicuspid pulmonary valve* is not uncommon with other cardiac anomalies, especially pulmonary stenosis and hypoplasia of developmental origin, but it is rare as an isolated lesion. There are 64 cases from the literature in Dilg's statistics, and 24 others in our series, of which latter in 4, 1 by Sir James Paget and 3 by Martinotti and Sperino, a bicuspid pulmonary valve was the only anomaly, while in the remaining 20 cases it complicated other defects. This makes a total of 88 cases in the literature, in 5 of which, 2 in Dilg's series and 3 in ours, the aortic valve was also bicuspid.

Bicuspid Aortic Valve.—This is of much clinical interest, both because of the great tendency to become the seat, first of a sclerosing, and then of a subacute bacterial inflammatory process, and because of the strain upon the posterior wall of the aorta, which not infrequently ruptures, or shows the degenerative changes preliminary to the formation of a dissecting aneurism. Bicuspid aortic valve usually occurs alone or in association with coarctation and hypoplasia of the aorta, or (less commonly) with certain other minor anomalies, such as subaortic stenosis, patent ductus arteriosus, persistent left superior vena cava, defect at the base of the interventricular septum, congenital aneurism of the right aortic sinus, etc., which appear to belong in the same complex as due to arrest at a fairly late period of gestation, *i. e.*, just before the aortic and interventricular septa have been completely closed.

¹ *Montreal Gen. Hosp. Repts.*, 1880, 1, 233.

³ *At. d. R. Ascc. d. med. d. Torino*, 1884.

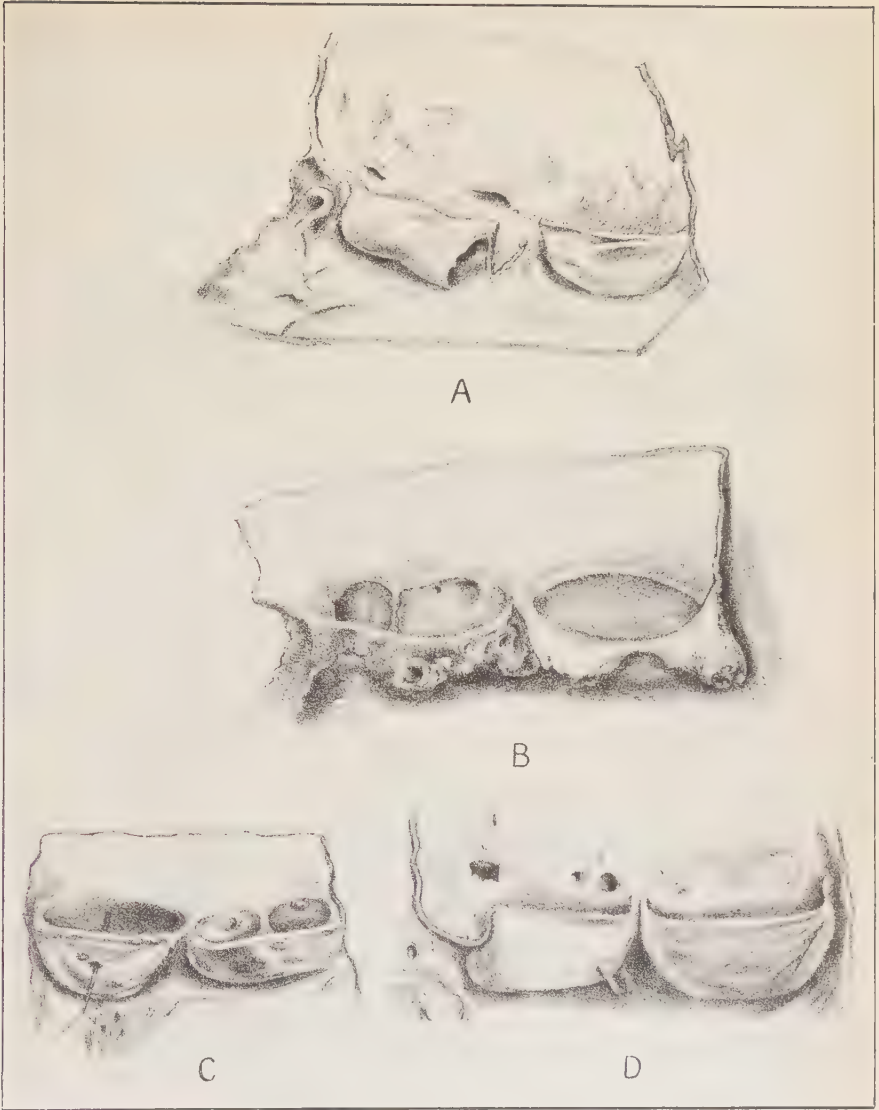
² *Virchow's Arch.*, 1883, 91, 192.

⁴ *Gaz. del. clin. Torino*, 1886.

In some instances both pulmonary and aortic valves may be bicuspid. The anomalous segments may be large, with smooth surfaces, showing no sign of further division, a true reduction in number existing; or one or both may present on the arterial aspect a low ridge or raphé imperfectly dividing the sinus behind it into two parts. Where such a raphé is absent, the condition is undoubtedly a true malformation, but where this exists, the origin of the bicuspid state of the valve admits of much discussion as to its postnatal (inflammatory) or congenital origin. Peacock arrived at the conclusion that the majority of cases were congenital, due either to an original malformation or to fusion in a fetal endocarditis.

Osler,¹ in 1886, published a statistical study of 18 cases of bicuspid aortic valve, and enumerated the following points as arguing for a probable congenital origin of the fusion, or imperfect division, of the combined cusp: (1) The presence of a low or partly obliterated raphé behind the conjoint cusp; this occurred with greater or less prominence in all his 18 cases. (2) Compensatory changes in the cusps of the nature of enlargement of the single, or shortening of the combined cusp, so that the free margin of the latter is equal to, or shorter than, or only a little longer than, the single segment; in 7 of his 18 cases which admitted of careful measurement, the combined was equal to the single cusp in 1 case, shorter in 2, and somewhat longer in 4 cases, and the latter appears to be the rule, from Deteindre's statistics. (3) The relative frequency, in the majority of cases of the union of the anterior and left posterior, right and left coronary segments. This occurred in 16 of the 18 cases and was apparent in all the statistics of later writers, but has been shown by Lewis and Grant, to be characteristic also of cases of inflammatory fusion. (4) The ventricular surface of the combined cusp toward its attached border is usually free from sclerotic changes such as must occur in inflammatory fusion and there was commonly a slight indentation here marking the point of junction of the combined cusps. (5) Other anomalies of the aortic cusps occur which favor the possibility of a congenital origin of the raphé, behind the combined segment. Thus in one case in his series two of the cusps were connected with each other and with the aorta by a median raphé, and in addition there were three strong *chordæ tendineæ* 7 cm. in length, thin and free from any trace of inflammatory thickening, which united the edge of the valve to the aorta to which they were attached at the normal level. This finding is important in the light of the suggestion made by Wilks and Moxon, that congenital fenestrations of the aortic cusps are a reversion to the stage seen in certain dipnoan fishes in which the several rows of valves in the conus arteriosus are attached by long fenestrated *chordæ tendineæ* to the aortic wall above them. All the cases reported by Osler, except 1, a fetus at seven months with multiple associated anomalies and bicuspid aortic and pulmonary valves, were in adults, and in all but 2 the cardiac condition was the cause of death and the valves were sclerosed and bore traces of old inflammation. In 8 cases they were also the seat of acute inflammatory change and the tendency of these anomalous cusps to disease was stressed by Osler and the earlier writers.

¹ *Trans. Assn. Am. Phys.*, 1886, 1, 185.



Reproduction of Plate IX from the *Montreal General Hospital Reports*, 1880, illustrating Sir William Osler's article on "Malformations of the Semilunar Valves." The plate shows cases I, II, IV, and V of the Reports, which are also tabulated in his article "On Bicuspid Conditions of the Aortic Valve," *Trans. Assn. Am. Phys.*, 1886, 1, 191, as Nos. 3, 4, 1 and 6 respectively. All four specimens are in the Pathological Museum of McGill University. (a) Fusion of anterior and left posterior cusps. Single and combined segments of equal length. From a man aged twenty-six years, who had worked as a blacksmith, and died of cardiac dropsy. Case I in *M. G. H. Reports*, No. 3 in *Transactions*. (b) Fusion of anterior and left posterior segments. Recent vegetation. Prominent raphé. Fused longer than single segment. From a man aged twenty years, who died suddenly of cerebral aneurism. Case II of Reports, No. 3 of *Transactions*. (c) Fusion of anterior and left posterior segments. Single cusp 1 cm. longer than conjoint segments. V-shaped deficiency in united curtain. From a man aged forty-two years, dying of cardiac dropsy, after five months illness. Case V in Reports, No. 1, in *Transactions*. (d) Fusion of anterior and right posterior segments. Valvular aneurisms, vegetative endocarditis and calcification. From a man aged forty-five years. Case I in Reports, No. 6 in *Transactions*. Note the absence of raphé in Fig. A and Fig C, and the situation of this in Figs. B and D.

Parkes Weber¹ pointed out that, while in some of these cases the lesion might be a congenital fusion due to a fetal endocarditis, in others it must be developmental due to a primary arrest of growth and that the presence of associated anomalies (as suggested by Sir Archibald Garrod²) might assist in establishing this, as well as the form of the raphé behind the conjoint cusp, which, in one of his cases was much fenestrated along its

FIG. 86



Bicuspid aortic valve of congenital origin due to fusion of the anterior and left posterior (coronary) cusps. Low calcified raphé behind these and lengthening of the single cusp which is 1 cm. longer than the fused segment. Aneurismal dilatation of the posterior wall of the aorta behind the single segment with fissuring of intima and formation of dissecting aneurism round base of heart and spontaneous rupture of this into the pericardium. (From a specimen in the McGill Museum, presented by Sir F. Andrewes through Dr. C. F. Martin.)

free border, a proof of its developmental origin. That the raphé behind the conjoint cusp may be the result of a true arrest of growth has been clearly demonstrated by Lewis and Grant.

That many cases of bicuspid aortic valve are the result of postnatal inflammatory fusion may be reasonably surmised when: (1) The compensatory changes in the length of the fused cusp have not taken place, so

¹ *St. Bartholomew's Hosp. Repts.*, 1899, 35, 147.

² *Ibid.*, 1894, 30, 53.

that its free margin is considerably longer than the single cusp; (2) when the raphé dividing the sinus of Valsalva behind it has its superior origin on a level with the superior origin of the unaffected cusp, instead of at a lower point in the aortic wall or on the floor of the sinus; (3) when in addition the only thickening observable is in the angle between the fused cusps indicating a progressive fusion beginning at the fixed and relatively motionless point, the aortic wall (Adami).

Sir Thomas Lewis and R. T. Grant studied histologically by serial sections and reconstruction, 11 cases of congenitally bicuspid valve, 7 of which were the seat of superimposed infective process, and compared these with normal cusps and with 2 cases of inflammatory fusion. A statistical survey was also made of 116 supposedly congenital cases from the literature, of which 33 were accepted as unquestionably congenital. The histological studies showed that, in the cases of partial subdivision, the low raphé behind the conjoint segment (which as Osler pointed out was evidence of a congenital origin), is not an incomplete fusion, but a true malformation, an arrest of out-growth of the annulus fibrosis and covering layers of the valve, so that the several normal layers of one cusp pass uninterruptedly into those of the other across the region normally broken by the commissure. A further conclusion drawn from these studies, is that a congenitally bicuspid valve is especially prone to and often *determines the onset* of an infective endocarditis, which occurred in 23 per cent. of the males reaching adult life in their series.

Atheromatous changes at the base of the aorta have been frequently noted, and in 6 of the 11 cases described by Babes and Deteindre there was an aneurismal bulging of the right posterior wall of the aorta, which formed in 5 instances a definite aneurism, from the rupture of which, in 2 cases, death ensued. This is seen also in 2 cases in the McGill Museum.

Cases of bicuspid aortic valve not included in any of the published series have been reported by Shelby¹ and Baumgartner.²

Total Incidence.—Osler's 18 cases of bicuspid aortic valves occurred in 800 personal autopsies, and Lewis and Grant found this condition 3 times in 215 autopsies in which they examined especially for it, while de Vries found it in 12 cases among 3600. These figures supply a fair statement of the average relative frequency. If we add to the 116 cases collected by Lewis and Grant and subclassified by them as "actually of congenital origin" (33 cases), and "mainly congenital" (83 cases), 53 others in our series not included in their statistics nor covered by their bibliography, the total is 169 cases of bicuspid aortic valve in the literature to date, of which 70 may be pronounced to be of congenital origin and 99, in their phraseology, are "mainly" or probably congenital.

The associated anomalies in the additional cases in our series complicating other defects are of interest, especially when compared with the similar figures in the 33 cases of congenital origin tabulated by Lewis and Grant. In the 25 cases in our series complicating other defects and not included in theirs, 1 case was associated with pericardial defect;

¹ *Trans. New York Path. Soc.*, March 10, 1897.

² *Clifton Med. Bull.*, 1923, p. 17.

1 with congenital rhabdomyoma; 4 with defect at the base of the inter-ventricular septum; 3 with communication between the base of the aorta or aortic sinus of Valsalva and pulmonary artery; 2 with partial transposition of the great trunks; 2 with pulmonary stenosis; 1 with pulmonary atresia; 3 with patent ductus arteriosus; and 8 with coarctation of the aorta. In Lewis and Grant's series 27 of their 33 (which include the majority of our cases "classed as the primary lesion") were with associated anomalies; these were pulmonary stenosis in 2 cases, ventricular septal defect in 3 cases, coarctation of the aorta in 11 cases, anomaly of the great vessels in 4, and in 7 cases the pulmonary valve was also bicuspid with or without other congenital defects.

Miscellaneous Anomalies.—Dilg reports a remarkable case, in a child aged two years, of an endocardial fold divided roughly into two cusps with their convexity toward the ventricle, just below the base of a bicuspid aortic valve, both coronaries being behind one cusp. Banks¹ reported a woman, aged thirty-four years, with physical signs of aortic insufficiency and a loud, musical murmur at the base, audible at some distance from the chest, whose heart was hypertrophied and presented a cribriform condition of the aortic valve, and one-quarter inch below it in the left ventricle three other rudimentary cusps. These may be of compensatory, postnatal origin, as in a number of other cases recorded of long-standing aortic insufficiency.

In one of Babes' cases of bicuspid aortic valves, a peculiar band, like a papillary muscle of the mitral valve, traversed the sinus of Valsalva. Hektoen² quotes from the literature several other instances of anomalous cords at the level of the valves, and a case observed by himself of a large defect at the base of one of the segments, all of which he ascribed to defects in the development of the aortic septum.

Defective Development of the Semilunar Cusps.—In a few instances of bicuspid valve a gap may be left on the wall of the vessel between the segments where evidently no third cusp has formed. This occurred in two of Deteindre's series. A remarkable instance of such a defect in the pulmonary valve is recorded by Stinzing. Here there are only two pulmonary cusps, and a large free space occupying the position of the third was traversed by two low ridges, evidently its rudiments. The heart was from a woman, aged sixty-four years, presenting signs and symptoms of pulmonary insufficiency.

The *fenestrations* so often seen above the line of closure of the semilunar cusps are thus explained by Wilks and Moxon: "We have seen them in young people and we have always regarded them as congenital, for in some of the lower animals the sigmoid valves are attracted to the artery by thin tendinous cords, in the same way as the auriculo-ventricular. You may see this in the heart of the shark."

PRIMARY DEFECTS OF THE AURICULO-VENTRICULAR ORIFICES

Congenital disease of the auriculo-ventricular valves differs from that of postnatal life chiefly in its infrequency, in the more extreme character

¹ *Dublin Hosp. Gazette*, 1857, p. 330.

² *Chicago Path. Soc.*, 1905.

of the process, atresia being more common than stenosis, and in the fact that the right side of the heart is usually affected rather than the left. Owing to the rarity of the cases, to the short duration of life, and to the fact that in the infant heart the picture presented is hard to distinguish from that of the more frequent lesions at the arterial ostia, this subject is not of great clinical importance, and its chief interest lies in the contribution which it brings to our information upon the question of the pathogenesis of cardiac defects.

Tricuspid Stenosis.—Although this lesion is not very uncommon in adults the cases which can be proved to have originated in intrauterine life are very rare. Vierordt knew of only three instances, unassociated with disease of the pulmonary valves, in the literature. In combination with pulmonary stenosis or atresia it is more frequent. A good illustration of the latter combination is seen in a specimen in the McGill Museum, presented by Sir William Osler. In the heart of a cyanotic infant aged four months, both pulmonary and tricuspid valves are thickened, shortened, and fused, and their orifices markedly reduced; the ventricular septum is entire, the foramen ovale widely patent, the right auricle hugely dilated, and the tricuspid surmounted by recent vegetations. Such cases are undoubtedly of inflammatory origin, and are of value as proving that fetal endocarditis, although it has been overrated as a cause, certainly has its place as an etiological factor in congenital cardiac disease.

Tricuspid Atresia.—Although in itself rare, tricuspid atresia is the commonest of all congenital lesions of the auriculoventricular cusps. Rauchfuss collected 16 cases from the literature of which 5 were due to a defect in development, 5 were apparently inflammatory, and the remainder were of "doubtful" origin. Since then additional cases have been reported by Chapotot (quoted by Vierordt), Sieveking, Kühne¹ (2 cases) Bernstein,² Wieland,³ Hedinger,⁴ Corsdren⁵ and Miller.⁶

Pathological Anatomy and Pathogenesis.—Cases of inflammatory origin must be distinguished from those due to a defect in development. Those of inflammatory origin have usually progressed through a stenosis and show distinct evidence of an antenatal valvulitis in the form of an extensive cicatricial contraction of the endocardium adjacent to the obliterated tricuspid orifice, and often of the pulmonary valves. The developmental cases, on the other hand, may present no sign of inflammation, but the tricuspid orifice is absent, and either shows no trace of its presence, or this is marked by a shallow groove, the tricuspid segments are lacking, and the right auricle is divided from the right ventricle by a thick muscular septum. Kühne, and subsequently Wieland, subdivided these developmental cases into a group of (a) "isolated" primary atresias in which certain pathological changes of a secondary nature are constant so that a definite type is set up, and (b) tricuspid atresia complicated by other grave cardiac anomalies of independent origin, such as transposition of the arterial trunks, pulmonary atresia, etc. Eight cases of the "isolated" form that constitutes the first group were separated by Kühne,

¹ *Jahrb. f. Kinderh.*, 1906, **63**, 235.

² *Jahrb. f. Kinderh.*, 1914, **79**, 320.

³ *Monats. f. Kinderh.*, 1924, **28**, 193.

⁴ *New York Path. Soc. Reports*, February, 1906.

⁵ *Centralbl. f. allg. Path.*, 1915, **26**, 529.

⁶ *Am. Jour. Path.*, 1925, **1**, 467.

and later by Wieland, from the others. To these may be added one by Bernstein from our series. The changes in all of these are practically identical and clearly indicate the sequence of events. There is an entire absence of the tricuspid orifice, and the body of the right ventricle is an aplastic structure, while the left is highly hypertrophied and dilated, appearing at first sight to form the whole heart, with the right chamber as an appendage to it; the right auricle is also hugely dilated and the foramen ovale is widely patent, or a defect of the interventricular septum exists; in addition there is always a defect in the muscular interventricular septum leading from the cavity of the left ventricle into the dilated conus of the right ventricle and thence into the pulmonary artery. The course of the circulation is necessarily from right to left auricle through the foramen ovale, and thence to the left ventricle, from which the blood is distributed in part to the aorta and in part through the septal defect to the pulmonary artery. The aorta is usually dilated, and the pulmonary is normal or somewhat reduced in size owing to the smallness of the chamber from which it springs.

These cases of "isolated primary tricuspid atresia" show that the old mechanical or congestive theory of septal defects in pulmonary stenosis, in which the defect was thought to be secondary to the raised pressure in the right ventricle, must be accredited here. That is to say, the septal defect in tricuspid atresia is here evidently secondary to the congestion in the left ventricle which forces an outlet in the conus of the pulmonary artery and this allows the circulation to be maintained. Wieland points out and insists on the importance of Kühne's separation of this group, with its constant secondary complex, on this account.

Cases of developmental tricuspid atresia with aplastic left ventricle constitute one well recognized form of the *cor biatriatum triloculare*. Where transposition of the arterial trunks is associated, as in Hedinger's case, the circulatory conditions are favorable and life may be prolonged past middle age. Here, as Corsdren has pointed out, the circulation was practically identical with that in the heart of a frog, the aerated blood from the left auricle entering the aorta in advance of the venous blood from the right auricle, which had to pass through the opening in the auricular septum and the chamber of the left auricle, before it arrived in the ventricular part of the heart for distribution through the aorta, which arose to the right and anteriorly, and the pulmonary artery, which lay to the left and posteriorly, and was stenosed at its orifice, although dilated above this.

Etiology.—The causation of the cases of inflammatory origin is that of fetal endocarditis elsewhere. In tricuspid atresia a secondary ventricular septal defect is bound to occur, for the proper maintenance of the circulation, as well here as in the developmental forms.

Much interest attaches to the causation of the developmental forms of tricuspid atresia. In the embryo the auricular canal opens at first by a common orifice into the left side of the common ventricle, and later by a process of shifting to the right comes to lie more in the median line. The theory had been advanced that either a lack or an exaggeration of this shifting to the right would lead to a wrong adjustment of the parts,

and to a mitral or tricuspid atresia. Again, the auriculoventricular orifice is divided into the mitral and tricuspid ostia by the growth of endocardial cushions in its centre, and by a union of these with the interauricular and interventricular septa. Should these cushions become deviated to the right or to the left in their formation they may become adherent to the corresponding wall of the common ostium and thus lead to tricuspid or mitral atresia. Rokitsansky thus explains his case of mitral atresia. In that by Robertson the tricuspid atresia present was ascribed to a fusion of the endocardial cushions with the malposed auricular secondary septum, in consequence of a persistence of the *valvulae venosae* which formed a coarse network across the cavity of the right auricle. The suggestion has also been made that a premature obliteration of the ductus arteriosus during early fetal life, might lead to aplasia of the right ventricle and tricuspid orifice by cutting this part of the heart out of the fetal circulation. This possibility is disproved, however, by the fact that in several of the cases this passage is freely patent. The conclusion remains that the probable causation of mitral and tricuspid atresia lies in the mal-position and irregular union of those parts of the cardiac septa dividing the mitral from the tricuspid ostium.

Symptoms and Signs of Congenital Tricuspid Stenosis or Atresia.—Cyanosis may be present from birth or develop after a few days or weeks. In the classical developmental type described above it is usually extreme in the end, though its onset may be delayed. In Bernstein's case, aged two years and eight months, it did not appear until the sixteenth month, but then became marked with clubbing, and a polycythemia of 10,000,000 developed. This late appearance was possibly explained by the absence in this case of the auricular septum, a condition which must have facilitated the circulation. Kelley's patient a delicate child, showed only slight lividity on crying or when he had a cold, and in Sieveking's case, dying at nine weeks, cyanosis was absent throughout, but dyspnoea was prominent. The most remarkable instance of absence of cyanosis occurred in Hedinger's patient, a woman, dying at the age of fifty-six years, who could dance and mountaineer with ease, and who showed no cardiac symptoms whatever, except an occasional slight blueness of the lips. She became pregnant and abortion was done for generalized oedema and dyspnoea which were immediately relieved. Death took place several years later from failing compensation with marked terminal cyanosis. Dyspnoeic attacks are prominent, often of daily occurrence and are frequently the direct cause of death.

Physical signs are not very characteristic, being obscured by those of the septal defect that in tricuspid atresia is always present, and by the fact that a systolic murmur with maximum intensity over the right ventricle, such as is usually produced in these cases, may with difficulty, be distinguished from one generated at the pulmonary area. The marked hypertrophy of the left combined with the smallness of the right ventricle is of assistance in the differential diagnosis from pulmonary valve disease, although allowance must be made for the increased cardiac area produced by dilatation of the right auricle. This feature was indicated

in Wieland's patient by a zone of dulness to the right of the vertebral column behind. His case was characterized also by a strong systolic murmur and precordial thrill of maximum intensity at the apex, both of which were of a *curiously intermittent character*.

Duration of Life.—Most of the developmental cases of tricuspid atresia do not live more than one year. Bernstein's patient reached two years and eight months, a relatively high age perhaps explained by the almost complete absence of the interauricular septum that was present. Where transposition of the great trunks is also associated, as in the case reported by Wayne Bissell,¹ and in that by Hedinger, the circulation is greatly facilitated and life may be maintained, as shown by the latter case, into the sixth decade.

Congenital Mitral Stenosis.—"Pure" mitral stenosis in children or young adults without any previous history of infection has been ascribed, especially by the French writers, to prenatal disease, and probably a few of the cases, especially those associated with a widely patent foramen ovale may have so originated although in these latter cases the forcing apart of a valvular patency under the raised pressure in the left auricle may frequently be assumed in cases of postnatal origin. A curious combination of dwarfism and mitral stenosis in patients who have attained adult life has been observed. L'Abbé reports a case in a woman, aged twenty-seven years, of extremely small stature (1 meter high, 43 kilos weight), puerile intelligence, and marked infantilism. There was no doubt of congenital syphilis and a pure mitral stenosis.

Mitral stenosis in young infants, due either to an antenatal valvulitis or (more frequently) to a definite arrest of development of the parts entering into the formation of the left auriculo-ventricular orifice presents a very distinctive picture, owing to the marked compensatory changes in the heart and great vessels, the left ventricle aplasic with rudimentary aorta, the left auricle and right chambers greatly enlarged and the dilated pulmonary artery forming the aorta through a greatly dilated ductus arteriosus. The subject has been reviewed by Donnally,² who reported a typical case in an infant aged fifty-seven hours and collected 11 cases from the literature with ages from a few weeks to three and a half years. Cyanosis and dyspnoea had been present in all the patients from birth, and in Carmichael's patient, who lived to three years, there was clubbing as well.

Mitral Atresia.—A complete obliteration of the mitral orifice is still rarer than stenosis, and here a developmental origin may more constantly be assumed. A series of 12 cases was collected by Dudzus³ in which mitral atresia is associated with complete absence of the ventricular septum (cor biatriatum triloculare). A thirteenth case of this complex has been added by McIntosh⁴, in an infant aged five weeks. The left auricle and ventricle were aplasic and the right auricle and right side of common ventricle were hugely dilated, the great trunks arose in normal

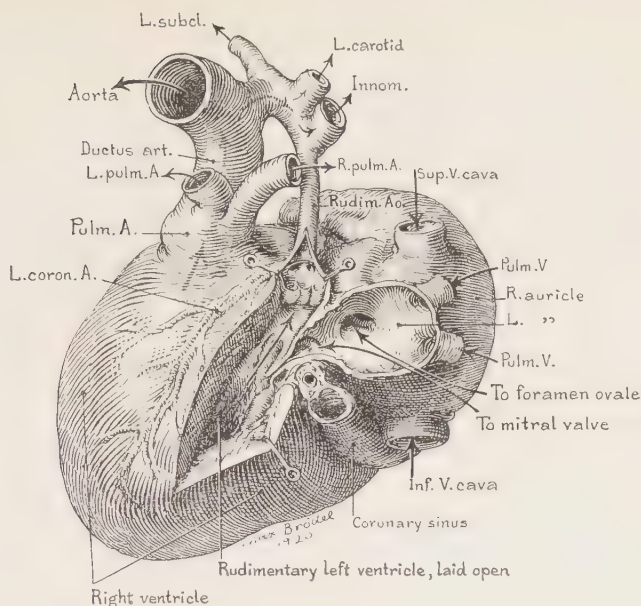
¹ *Tr. Chicago Path. Soc.*, 1913-1915, **9**, 159.

² *Jour. Am. Med. Assn.*, 1924, **83**, 1318.

³ *Virchow's Arch. f. path. Anat.*, 1922, **37**, 32.

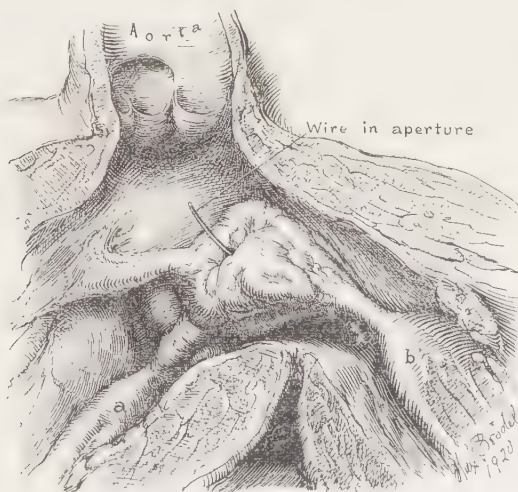
⁴ *Am. Heart Jour.*, 1926 (in press).

FIG. 87



a

a. Mitral stenosis of developmental origin showing aplasia of left ventricle with perfectly formed aortic cusps and rudimentary aorta. Pulmonary artery forming descending aorta, hypertrophy and dilatation of right chambers.



b

b. Magnification 10 diameters of the congenitally stenosed mitral valve, showing wire in aperture and puckered baggy valve with papillary muscles and rudimentary chordæ. (Dr. H. H. Donnelly, *Jour. Am. Med. Assn.*, 1924, 83, 1318.)

relations, and, as in Donnally's case, the pulmonary artery formed the descending aorta through the greatly dilated patent ductus; the auricular septum was completely closed, but one of the right pulmonary veins entered the superior cava and an *anomalous vessel connected the latter with the left auricle and formed the only means of communication between the aerated blood entering the left auricle and the chambers of the heart*. The marked cyanosis cleared up remarkably on administration of oxygen. The same remarks apply in regard to etiology as in tricuspid atresia, but here a primary defect in development may be almost constantly assumed. Grave associated anomalies are also nearly always present, and give additional proof of a teratological origin. In Thérémín's observation of an infant aged two days, the left auricle and ventricle were aplasic without any trace in the latter of a mitral orifice, its walls being formed throughout of finely reticulated muscle fibres; the foramen ovale was closed, the interventricular septum defective, the pulmonary valve bicuspid, and the aorta appeared to arise from the right ventricle; there was a *horseshoe kidney and double ureter*. Lawrence and Nabarro give a similar case of mitral atresia, defect of the septum, aplasic left ventricle, the aorta arising behind the pulmonary artery from the right ventricle, with *coarctation of the aorta, transposition of the stomach, absence of spleen and hepatic section of inferior vena cava; anomalies in form of liver and lungs*.

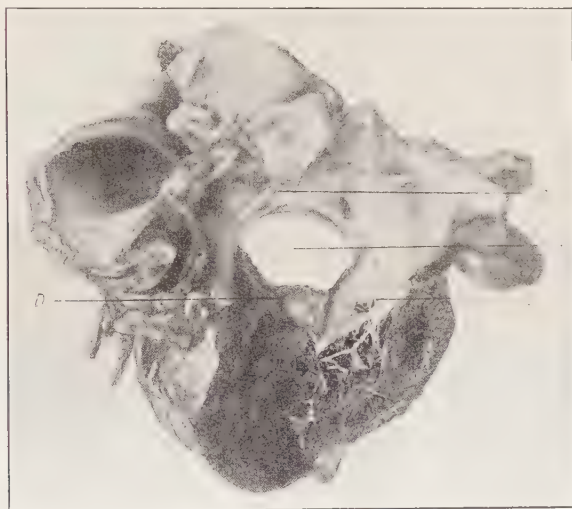
Congenital Mitral and Tricuspid Insufficiency.—These lesions may result from a primary malformation of the cusps or from secondary deformity in the arrest of development of neighboring structures, as in persistent ostium primum or defect of the ventricular septum at the base. Or they may be due to thickening and shortening of the valve in a fetal endocarditis; thus Barth and Roger describe a case in which, on auscultation before birth, a long, loud, rough murmur was heard accompanying the heart sounds. The child was stillborn three days later, and the right ventricle was found dilated, the tricuspid orifice enlarged, and its cusps shrunken and insufficient, and evidently the seat of an endocarditis. In the case of Steffen, of a child aged ten and a half months, the tricuspid segments were replaced by a low ridge which was thickened, reddened, and slightly jagged. The mitral cusps were similarly thickened and reddened, and one of them was reduced likewise to a narrow ridge. The tricuspid valve was congenitally defective in one or more of its segments in 2 cases reported by Hotz¹ of two children aged twelve and thirteen years. The right chambers and pulmonary artery were greatly dilated and there was a widely patent foramen ovale. One case ended with marked cyanosis; paralysis of the recurrent laryngeal nerve and diminution of the left arterial pulse occurred as a result of pressure upon the nerve and the aortic arch by the greatly enlarged pulmonary artery which showed under the roentgen-ray as a bulging widely pulsating arc. Steffen's case is the only instance of congenital mitral insufficiency found in the literature.

¹ *Jahrb. f. Kinderh.*, 1923, **102**, 1.

ANOMALIES OF THE AURICULO-VENTRICULAR CUSPS

Double Auriculo-ventricular Orifice.—A second valvular opening supplied with its own cusps, chordæ tendineæ and papillary muscles, may be within the segments of an otherwise normal auriculo-ventricular valve. Seven such cases are recorded, 6 of double mitral orifice by Greenfield,¹ Cohn,² Degen,³ Stuhlenweisenberg⁴ and Camisa,⁵ and 1 of double tricuspid by Pisenti.⁶ In Stuhlenweisenberg's case, and in one of Camisa's, the two orifices were of equal size, and were separated by a bridge of valve tissue which supplied a cusp to either opening; in all the other cases the second opening was much smaller, and lay in one of the segments of the primary orifice.

FIG. 88



Heart of a child, aged five years, showing; *A*, defect of lower part of interauricular septum; *B*, patent foramen ovale; *C*, double mitral orifice; *D*, cleavage of mitral segment. (From a specimen in the Pathological Museum, McGill University.)

Two cases of the latter description are in the Harvard and the McGill Medical Museums. In the Harvard case, an opening 2 cm. long lies in the aortic cusp of the main mitral orifice, and leads into an aneurismal pouch formed by the apex of this segment, which communicates with the cavity of the ventricle by numerous fenestrations. The McGill heart (Fig. 88) is of bizarre external form owing to its bifid apex, deep auriculo-ventricular groove, and hypertrophied right chambers. The interauricular septum presents a small valvular patent foramen ovale above, and is absent in its lower two-thirds, a large crescentic defect (*persistent*

¹ *Trans. Path. Soc.*, 1876, **27**, 128 (with plate).

² *Inaug. Dissertations*, Königsberg, 1896 (with plate).

³ *Inaug. Dissertations*, Griefswald, 1903.

⁴ *Centralbl. f. Pathol.*, 1912, **33**, 1027.

⁵ *Di una rarissima Anomalia della tricuspid*, Perugai, 1888.

⁶ *Ibid.*, p. 342.

ostium primum) existing. The mitral valve is replaced by a single large segment which is cleft in its anterior portion, passing forward from either side to be inserted into the middle of the base of the interventricular septum where this bounds the interauricular defect below. The secondary mitral ostium lies in the posterior half of this large primary segment, 7 mm. back from its free margin. It is a perfect valvular opening admitting a lead-pencil with two well-formed cusps attached to slender chordæ, arising from two short papillary muscles which lie behind and independent of the single group from which the chordæ of the primary segment spring. The right auriculo-ventricular valve is malformed and an irregular excavation in its septal cusp suggests an unsuccessful attempt at a double tricuspid ostium. The aortic valve is bicuspid. The endocardium is healthy.

Etiology.—Camisa believed a fetal endocarditis had led to a fusion of segments at their apices and to the formation of secondary orifices. Cohn and Stuhlenweisenberg suggest a malformation by excess, a view supported in the latter's case by the equal size of the two orifices. Pisenti supposed a fenestration of the endocardial cushions, which had transmitted the blood stream in early embryonic life and had become transformed into a second valvular orifice by a natural adaptation of growth, the papillary muscles and chordæ growing up to its borders.

In the two specimens seen by us, Pisenti's explanation seems to apply, the marked irregularities in both auriculoventricular valves due to the auricular septal defect in the McGill specimen, and the multiple fenestrations in the Harvard case, alike arguing for such accidental origin at an early embryonic period. Camisa's theory of a fetal endocarditis is not tenable in the case of the McGill specimen and others in which the endocardium is free from every trace of sclerotic change.

Symptoms.—The double orifice is in itself of no clinical significance, the secondary segments functioning as normal valves. In the majority of the cases, including Cohn's patient, who died at seventy-one years, both sets of valves were thin, healthy and competent. Chronic endocarditis had supervened in both Camisa's cases and in Stuhlenweisenberg's. In the latter a loud systolic murmur over the precordium was associated with insufficiency and sclerosis of the segments of the *anterior* mitral ostium, the posterior remaining free.

Displaced Orifice.—A double mitral orifice is described by Andrewes,¹ in which two orifices separated by a fibrous septum lay one behind the other in the left ventricle. The right ventricle was rudimentary, the interventricular septum defective and the tricuspid valve absent. A deflection of the septum to the right so that both orifices are placed in the same ventricle was assumed.

Miscellaneous Anomalies.—Various minor defects, as irregularly formed or accessory leaflets and anomalous arrangement of the chordæ tendineæ or papillary muscles occasionally occur, and may in some instances contribute to an insufficiency of the valves.

¹ *Trans. Path. Soc.*, London, 1903, vol. 54.

PRIMARY PATENCY AND ANOMALIES OF THE DUCTUS ARTERIOSUS BOTALLI

The ductus arteriosus of the fetus is a short, thick trunk, 10 to 15 mm. long, running from the left branch of the pulmonary artery directly after the bifurcation to the under side of the arch of the aorta just beyond the origin of the left subclavian artery, which serves to carry the unaërated blood, returned from the head and upper extremities, to the descending aorta, whence it passes to the placenta. At birth the ductus undergoes a rapid involution, its lumen becomes practically impermeable about the third week of life, the alterations in its wall, which lead to its permanent obliteration, going on for some months, and finally transforming it into the ligamentum arteriosum of later life. The average diameter of the patent ductus at birth is given by Vierordt as 5 to 6.8 mm. and by Thérémín as 4.8 mm. But when filled with fluid during life, or experimentally injected directly after death, it is found to be much larger. Thus in a series of infant hearts prepared by Klotz, in which he injected the ductus from the aorta with gelatin at autopsy, it was found in the newly born to be fully equal in size to the main pulmonary trunk. He ascribes its apparent smallness as usually seen postmortem to the firm contraction of the muscular wall.

The ductus may (1) remain patent throughout life, (2) undergo aneurismal dilatation, (3) it may be absent, or (4) it may have an anomalous origin or course.

Patency of the ductus is not infrequent in combination with other cardiac defects, especially those in which there is some serious interference with the pulmonary circulation. It occurred in 222 of this series of cases, in 30 of which it was combined with pulmonary atresia, in 21 with pulmonary stenosis, and in 42 with transposition of the great trunks, and in 66 with coarctation of the aorta. As an isolated condition it is among the more infrequent of cardiac anomalies. The first carefully recorded case of primary patency with autopsy findings, was diagnosed before death and published by Bernutz¹ in 1849. Six cases were collected by Almagro² in 1862, 12 by Gerhardt³ in 1867, 20 by Wrany⁴ in 1871, and 26 by Vierordt in 1898. Herxheimer enumerated all the above in 38 cases collected in 1910, while Wells,⁵ in 1908, found 41. A careful analysis of 34 cases with, and 37 without, autopsy report was published by Goodman⁶ in 1910, and there are important clinical studies by Hochsinger, Gillett,⁷ Taylor,⁸ and Wessler.⁹ The incidence of an acute infective process in patent ductus was discussed by Horder¹⁰ in 1908, and by Hamilton and Abbott¹¹ in 1914, who showed what appeared to be a primary involvement of the pulmonary trunk in a personal observation and in 10 other cases with infective endarteritis from the literature. In

¹ *Arch. gen. de méd.*, 1849, **20**, 415.

² *Thèse de Paris*, 1862, p. 67.

³ *Jena, Ztschr. f. Med. u. Naturwiss.*, 1867, Bd. 3.

⁴ *Oestr. Jahrb. f. Pädiatr.*, 1871, Bd., **1**, 1.

⁵ *Am. Jour. Med. Sci.*, 1908, **136**, 381.

⁶ *Univ. of Penn. Med. Bull.*, 1910, **23**, 509.

⁷ *Gaz. d. hôp.*, 1910, 83, p. 1419.

⁸ *Guy's Hosp. Gaz.*, May, 1901, p. 197.

⁹ *Am. Jour. Med. Sci.*, 1913, **145**, 543.

¹⁰ *Quart. Jour. Med.*, 1908-1909, **11**, 292 (Case 2.)

¹¹ *Trans. Assn. Am. Phys.*, 1914, **29**, 294 (gives full bibliography).

1915 an analysis of 64 cases of primary patency with autopsy reports from the literature was published by the writer in the *second* edition of this system. Other important contributions to the subject of infective pulmonary endarteritis complicating patent ductus have been made by Stoddard¹ (1915), Boldero and Bedford² (1924), and by Schlaepfer³ (1926) who added 7 additional cases from the literature to the 13 included in 1915 in Abbott's 64 cases. From all sources, the number of cases of primary patency with autopsy analyzed in our series from the literature or personal experience has been increased to 84, of which 20 are in "infants" under five years and 64 are in "adults" above that age. As of special interest, or not included by other writers, may be mentioned the cases by Hewitt,⁴ Hall,⁵ Kingsley,⁶ Thompson,⁷ and Carpenter⁸ in infants; and Kaulich,⁹ Fagge,¹⁰ Darier,¹¹ Schrötter,¹² Drasche,¹³ Garipuy,¹⁴ Crouzet,¹⁵ Greenhow,¹⁶ Gibson,¹⁷ Wells, Schnitzler, Mead,¹⁸ Josefson, Wasastjerna, Moench, Gerhardt,¹⁹ and Motzfeld²⁰ in adults.

Pathogenesis.—The causes of persistent patency of the duct are to be sought in the conditions of its normal closure, and this must depend upon the influences, mechanical or otherwise, of the changes in the circulation at birth, and upon the consequent alterations in the vessel wall, itself a fetal structure destined to involution. As *possible factors* in the process of closure may be enumerated: (1) peculiarities in the histological structure of the ductus wall, (2) alterations in the blood-pressure at birth, (3) modifications at birth in the position of the ductus relative to the aorta and pulmonary artery, and other mechanical factors preventing entrance of blood from the aortic side.

1. *Histology.*—The ductus wall is poor in elastic tissue as compared with the aorta and pulmonary artery, but is relatively rich in muscular elements, which, as well as the elastic tissue are known to undergo marked increase during the later months of intra-uterine life. More particularly a loose, subintimal layer of muscle is present (Thoma²¹); this evidently corresponds to Jore's musculo-elastic layer of the arterial wall, which is here developed both at an earlier period and to a greater extent than in the aorta and pulmonary artery. It is especially marked at either extremity of the duct where it can be seen to pass into and, indeed, to form, the musculo-elastic layer of the aorta (Klotz). When the canal is emptied of contents, as happens after birth, this increased

¹ *Arch. Int. Med.*, 1915, **16**, 38.

² *Lancet*, 1924, ii, 747.

³ *Trans. Path. Soc. London*, vol. **9**, 48.

³ *Arch. Int. Med.*, 1925, **37**, 473.

⁵ *Arch. Middlesex Hosp. Clin.*, Series XIII, 1913, p. 39.

⁶ *Johns Hopkins Hosp. Bull.*, 1911, **22**, 239.

⁷ *Edin. Hosp. Reports*, 1900, **6**, 57.

⁸ *Proc. Roy. Soc. Dis. Child.*, 1909, **2**, part 1, p. 163.

⁹ *Viert. f. prak. Heilk.*, 1862, **2**, 92.

¹⁰ *Guy's Hosp. Reports*, 1873, **18**, 22.

¹¹ *Bull. de la Soc. Anat. de Paris*, 1885, **10**, 55.

¹² *Ztschr. f. klin. Med.*, 1901, **43**, 161.

¹³ *Wien. klin. Wchnschr.*, 1898, **11**, p. 1195.

¹⁴ *Bull. de la Soc. Anat.*, February, 1907, p. 179.

¹⁵ *Ibid.*, 1869, **14**, 323.

¹⁶ *Clin. Soc. Trans.*, 1876, **9**, 152.

¹⁷ *Edin. Med. Jour.*, 1900, n. s., **8**, 1, 212, 436.

¹⁸ *Jour. Am. Med. Assn.*, December 24, 1910.

¹⁹ *Jena Ztschr. f. med. u. Naturw.*, 1867, **3**, Hft. 11.

²⁰ *Deutsches med. Wchnschr.*, 1913, **39**, 2037.

²¹ *Virchow's Archiv.*, 1883, **93**, 443.

muscularity enables it to contract firmly, so that its walls remain in juxtaposition and may undergo obliterative endarteritis.

2. *Alterations in the Blood-pressure at Birth.*—Previous to birth, the pressure is highest in the right side of the heart; the pulmonary arteries are small, and almost all the blood passes through the ductus into the aorta. At birth the lungs are expanded, their capillaries are opened, and there is an immediate lowering of pulmonary blood-pressure. It was suggested by Adami that during the first days of life the aortic tension, and therefore the mean blood-pressure in the body, is also lowered, owing to the reduced amount of work which the heart is called upon to perform, after the cutting off of the placental circulation, and that this reduction in the mean blood-pressure is the cause of the collapse of the ductus, and the main factor in closure. Kirstein also believes that a pressure equilibrium is established between the aortic and pulmonary circulations, which prevents a current through the ductus and thus permits of its obliteration.

3. *Mechanical conditions preventing the flow of blood through the ductus from the side of the aorta* have been adduced by many workers, and may reasonably be supposed to assist in the process of closure, especially when the pressure in the aorta comes to exceed that in the pulmonary circulation. Schantz supposed a stretching of the duct by the movement of the pericardium, pulmonary artery, displaced thoracic organs, and sternum, in the initial respiration, and Strassman described, on the basis of injection experiments, a fold in the aortic wall at the upper border of the mouth of the duct, which appears about the seventh month, and which he thinks closes its opening in a valvular manner when the pressure rises in the aorta at birth. This theory of a valvular aortic fold has been widely accepted and has received confirmation in the experimental work of Fromberg.¹ Nevertheless, its constancy in infants and its valvular action when present have been gravely disputed by such careful observers as Klotz,² and Kirstein and Stiènon.³ From the study of a large number of casts of the aortic isthmus and of patent ductus at various ages, Stiènon concludes that the essential mechanical factor in closure is the *dilatation of the fetal isthmus*, which is produced by raised aortic tension after birth, so that the latter has the secondary effect of favoring closure by pressure of the dilated isthmus on the aortic end of the duct. Dislocation of the thoracic organs in the establishment of respiration probably also assists in diverting the circulation.

From the above considerations the general conclusion may be drawn that continued patency will occur (1) in conditions in which the blood pressure, either in the aorta or pulmonary artery, is maintained at a level approximating that before birth (as in atelectasis of the lungs), or in which, for any other cause, a high positive pressure in the ductus is maintained; (2) when a congenital defect in the structure of the ductus wall exists. That such a defect is not uncommonly the cause of patency is suggested by the frequent association of anomalies elsewhere and the not uncommon occurrence of a history of syphilis, or of anomalies

¹ Baumgar, *Arbeit. aus. d. Geb. d. Path.*, 1914, **9**, 198.

² *Trans. Assn. Am. Phys.*, 1907, **22**, 213.

³ *Archiv. de biol.*, 1912, **27**, 801.

in other members of the same generation, as in De la Camp's series of six brothers and sisters all with characteristic physical signs of patent duct.

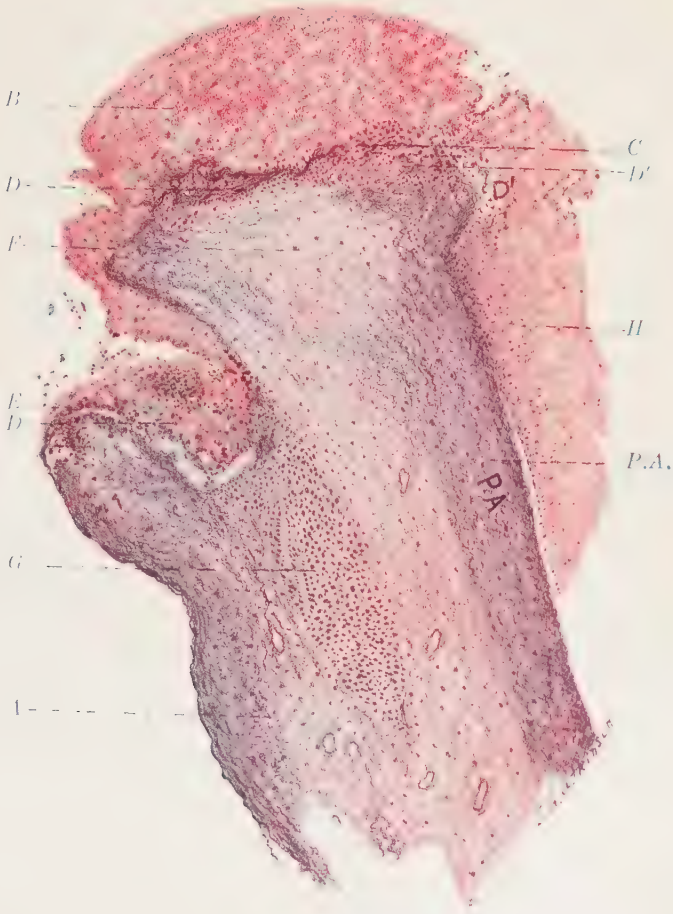
That raised pulmonary pressure is often at fault is evidenced by the frequent history of atelectasis of the lungs, difficulty in suckling or prolonged delivery in the mother, seen in the present series. In support of Stiènon's view, that dilatation of the fetal isthmus is an important factor, we may note that persistent patency is associated in most adult cases with a certain degree of coarctation of the aorta, and that the process of closure after birth is, like dilatation of the isthmus, a gradual one, extending over the first weeks of life and often not completed until the third month.

Pathology.—Three principal types of patency may be distinguished: (1) The duct may be greatly shortened upon itself so that its ends are approximated to each other, and it disappears as a canal, remaining as a simple aperture between the two great trunks. (2) More frequently the ductus persists as a short canal from 0.4 to 2 cm. long (Vierordt), with a lumen varying in size from one just admitting a bristle to one allowing the passage of a "goose-quill," "pencil," or even, as in Luys' case, the "finger." A patent ductus of long standing is usually shorter and broader than that of infancy or later fetal life. In form this canal may be (a) cylindrical, as is usual in infants, and as was seen in the cases by Fagge, Almagro, Gerhardt, and White¹ in adults; or (b) funnel-shaped (*i. e.*, conical, as in a funnel without a stem), with its larger end toward the aorta, as in a case by Murray, in which in a woman aged thirty-six years, it formed a truncated cone three-eighths of an inch long, just admitting a quill, and lying with its base to the aorta. Finally (following Gerhardt's classification into four types, of which the above forms 1, 2a and b constitute the first three), the patent duct may exist (3) as a canal which has undergone aneurismal dilatation.

In a patent ductus with otherwise normal conditions, the blood stream will be directed chiefly from the aorta, where the blood pressure is higher, into the pulmonary artery. This is evidenced by the funnel-shaped form with its base toward the aorta, which the canal usually assumes in adults, and by the presence of mycotic vegetations on the adjacent wall of the pulmonary artery in all the cases of acute infective endarteritis in the neighborhood of a patent duct. Wagener's 3 cases, in which the membrane at the pulmonary end bulged into the artery, also indicate this direction of the stream. Dilatation of the pulmonary artery, and hypertrophy and dilatation of the right ventricle, are usual results of patency of long standing. Rauchfuss thought them characteristic of all cases, but exceptions occur. The left ventricle may share in the hypertrophy and the aorta be moderately dilated. In Fagge's case, a woman aged forty-two years, the right ventricle was greatly hypertrophied, being equal to the left in thickness; the right auricle was dilated, and the main pulmonary branches, especially the right, were much dilated. The left ventricle is occasionally hypertrophied in excess of the right. In rare instances, as in Walsham's and Drasche's

¹ *Trans. Path. Soc.*, London, 1885, 36, 182.

PLATE VI



Microscopic appearances of wall of patent ductus and adjacent aorta and pulmonary artery in a case of patent ductus arteriosus with acute infective pulmonary endarteritis, showing site of initial lesion at pulmonary end of ductus. Drs. Hamilton and Abbott. (Colored drawing by Dr. J. H. Atkinson.) (Hem. and eos. and elastic tissue stains. Low magnification.)

A rectangular block has been cut to include the whole wall of the ductus (*D, D'*) and a portion of the pulmonary artery (*P.A.*, wall of pulmonary artery). *D, D'*, wall of ductus arteriosus in which the elastic tissue is almost destroyed, and which is surmounted by a thrombotic mass (*B*). *C*, pulmonary end of ductus, showing destruction of elastica, and organization of inflammatory products (*i. e.*, seat of initial lesion). *E*, aortic end of ductus showing zone of recent inflammatory exudate and invasion of tissue between aorta and pulmonary artery by acute inflammation. *F*, necrosed area below ductus wall. *G*, recent acute inflammatory process extending from aortic end of ductus into cellular tissue between aorta and pulmonary artery. *H*, thrombotic mass overlying wall of pulmonary artery and becoming incorporated with it in neighborhood of pulmonary end of ductus.

cases, aged respectively forty-seven and twenty-nine years, the heart may not be hypertrophied at all.

Atheroma and Rupture of Pulmonary Wall.—Arteriosclerotic patches are not uncommon in the neighborhood of the patent duct in the aorta, and extensive atheroma may occur also in the pulmonary artery. In Hebb's¹ case the atheroma and dilatation of this trunk seem to be explained rather by the obliteration of its left branch through the pressure of the thrombosed duct.

In a case recorded by Moench² in a woman, aged twenty-nine years, who died suddenly, the pulmonary artery presented an enormous dilatation of its anterior wall, which was the seat of a linear tear 2½ inches long rupturing into the pericardium; the patent ductus admitted the index finger and the pulmonary valve was bicuspid, which latter feature may have induced an element of strain. In Caylor's³ case of patent ductus, the rupture of a saccular aneurism of the ascending aorta had taken place immediately above a bicuspid aortic valve, and the vessel itself was the seat of a syphilitic mesaortitis.

Acute Infective Pulmonary Endarteritis.—Vegetations of a malignant character are not uncommon within a patent duct, about its aortic orifice, and on the adjacent wall of the pulmonary artery. There are 23 such cases in our collected series, in all the pulmonary artery adjacent to the ductus was extensively diseased and in all but 3, the heart valves were also involved in a malignant endocarditis. The 3 cases are of special interest because of the strict localization of the infective process to the ductus and the pulmonary artery adjacent, which showed clearly that the acute inflammatory process had originated in the immediate neighborhood of the defect, a point confirmed in 2 cases by microscopic examination, in which the organization of the inflammatory products proceeding at the pulmonary end of the ductus was clearly seen (see Plate VI), thus demonstrating this to have been in all probability, the earliest initial seat of a process, which had elsewhere and later assumed a fulminating, highly destructive character.

Hamilton and Abbott's patient, a girl of nineteen years, presented a clinical picture of septicaemia for some weeks before death, and the characteristic physical signs of patent ductus, without valvular involvement, or cyanosis. Postmortem a huge thrombotic mass of vegetations lay in the lumen of the dilated pulmonary artery blocking the orifice of a large patent ductus, and extending into the left pulmonary artery (see Fig. 89). The aorta was stenosed at the isthmus but was otherwise healthy and the endocardium of the heart was free from every trace of disease. Embolic abscesses in the lungs, the vegetations in the pulmonary artery, and the blood culture during life contained swarms of pneumococci. Both the patent ductus and pulmonary endarteritis were diagnosed during life. In Schlaepfer's case of a boy, aged eight years, presenting a loud rumbling continuous murmur in the pulmonary region with blood infection (*Streptococcus viridans*) and a history of double otitis media, the pulmonary

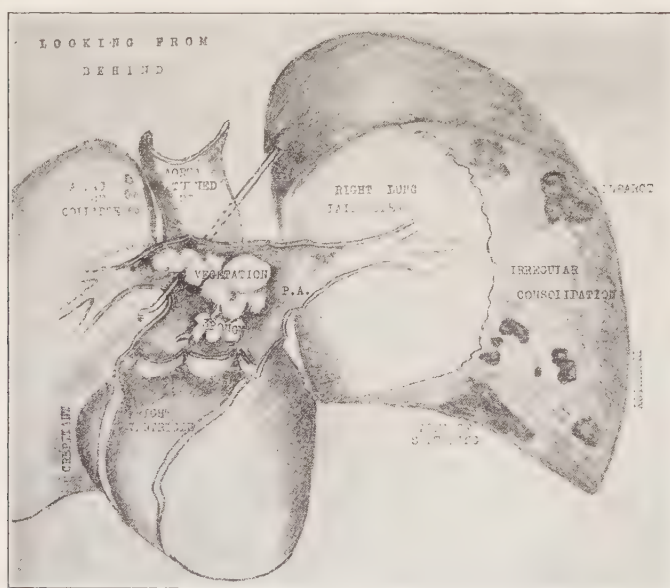
¹ *Trans. Path. Soc.*, London, vol. 44, 45.

² *Jour. Am. Med. Assn.*, 1924, 82, 1672.

³ *Tr. Chicago Path. Soc.*, May 13, 1918.

artery just above the valves was distended by a firm thrombus which extended into both its main branches and into the lumen of the patent ductus, but did not reach the aorta, and organization of the thrombus was found to be especially advanced at the pulmonary orifice of the ductus and on the anterior pulmonary wall and the lungs were the seat of multiple septic infarcts. Boldero and Bedford's patient, a man aged twenty-nine years, had a continuous murmur and thrill, with maximum intensity over the pulmonary area, and irregular fever. At autopsy, a massive vegetation was found completely filling the lumen of the pulmonary artery, extending from the valves, which were involved to slightly beyond the bifurcation and the patent ductus was filled with small warty

FIG. 89



Diagrammatic drawing showing acute vegetative endarteritis of pulmonary artery in the neighborhood of the patent ductus arteriosus, and consequent infarcts of the lung. A probe is seen passed through the patent ductus. (W. F. Hamilton and M. E. Abbott.)

vegetations, which protruded from its aortic orifice, the aortic cusps were also covered with luxuriant vegetations and there were small recent deposits on the mitral valves.

The wall of the aorta opposite the ductus was the seat of the mycotic vegetations in the cases of Hochhaus and Foulis, indicating that infection had proceeded in the direction of the reversed current through the ductus and had impinged here.

Paradoxical Embolism.—In Schmorl's¹ case, an embolus passed from a primary thrombus in the left auricle, through a patent ductus arteriosus to the pulmonary artery. In the cases of acute infective pulmonary

¹ *Verhandl. d. deutsch. path. Gesellsch.*, 1909, 13, 217.

endarteritis enumerated above, septic infarcts in both systemic and pulmonary circulations, evidently from emboli passing through the patent ductus, were extremely common, occurring even in those cases in which only the tricuspid valve and pulmonary artery were diseased. Hochhaus based a correct diagnosis upon this feature. In Stoddard's case, the infective inflammatory process appeared to have extended from the aortic valve through the ductus and down the adjacent pulmonary wall, and this author remarks that paradoxical embolism passing from left to right through the patent ductus is probably as frequent an occurrence as is the opposite course, from right to left auricle, through a patent foramen ovale.

Symptoms and Signs.—Clinical evidence of patency of the ductus is to be sought rather in physical signs than in symptoms, for the latter are often obscure. Nevertheless, their very negative character when taken in combination with the distinctly characteristic physical signs, presents, in the majority of cases, adequate grounds for a correct diagnosis, and this can almost always be made. A symptom complex has been built up which makes this chapter in congenital defects almost as legible as that of any form of acquired cardiac disease. On account of the secondary anatomical changes usually induced in patent ductus of long standing, such as shortening and widening of the duct and dilatation of the pulmonary artery, the picture in infants and early childhood is somewhat different and much less distinctive than that in later life. This statement applies especially to the physical signs.

The typical appearance is one of anemia, sometimes profound, which has been described as wax-like. Cyanosis is usually absent; when present it is generally slight and transient, appearing only on exertion, and usually develops late, sometimes as a terminal event. Of the 62 cases in which this point was mentioned, cyanosis was entirely "absent" in 27 (20 adults and 7 children under five years), and was "slight" in 7 cases, "terminal" in 17, and in 8 others "transient" occurring only in "attacks" as in Hale White's case (aged fifty-three years), or during crying, as in Simmon's case (aged sixteen weeks). In 2 cases only was it stated to be "moderate." Clubbing occurred in 5 cases of which only 1 had "moderate" cyanosis.

Dyspnoëic attacks usually accompanied by transient, but marked cyanosis, are relatively common in infants. Loss of consciousness may occur during the attack and the heart may stop beating, or death may supervene. Three typical cases were reported by Hall in infants, all of whom died during the attack, and others by Sanders, Luys, and Bommer.¹ In the last (aged sixteen weeks) the cyanosis was transient, coming on only during the attacks, which came on especially during feeding, and recurred at last so frequently that the child failed for lack of nourishment; during the attacks the breathing stopped suddenly and deep cyanosis developed, lasting two to four minutes; it passed off entirely as the breath returned, in the interval the color being normal. This is very suggestive of an admixture of venous with arterial blood as the cause of temporary cyanosis, the pressure becoming higher in the pulmonary artery and lower in the aorta during the act of suckling.

¹ *Freiburg Thesis*, 1900.

In older subjects cardiac seizures of various sorts may replace these suffocative dyspnoëic attacks. Paroxysms of extreme tachycardia (pulse 200), with dyspnoëa and bloody expectoration, lasting for some hours, and recurring every few months, are described in a man aged thirty-six years, with dyspnoëa and palpitation on exertion for years, but no cyanosis (Bommer). Hale White reports repeated angina-like attacks, in one of which death occurred, in a man aged fifty-three years, with a patent duct the size of the anterior tibial artery, but no hypertrophy of the heart or disease of this or of the aorta.

Epistaxis, hematemesis, and hemorrhages from other mucous surfaces are not uncommon (Almagro, Carmichael, Darier, Duroziez). Unless death occurs from some intercurrent condition, as malignant endocarditis or endarteritis, the patients usually die with failing compensation, and dyspnoëa is a remarkably constant feature. Sudden death occurred in 15 cases in our series; in 3 during dyspnoëic attacks, in 7 without apparent cause, in 1 case from rupture of the heart and in 2 from rupture of a pulmonary aneurism.

Physical Signs are almost invariably present, and are usually characteristic in older patients. In infants they are practically indistinguishable from those produced by auricular and ventricular septal defects. This is because the patent duct is at first a straight canal, which does not allow of the passage of a large volume of fluid and because in the absence of dilatation of the pulmonary artery there is less sound produced by the impinging of currents in this situation. Among our 84 cases physical signs were absent in only 8 cases. Absence of physical signs in the case of Walsham must be pronounced doubtful, for the specimen came from the dissecting-room with an indefinite note that cyanosis and pericardial murmurs existed. A negative finding in the cases by Luys and Duroziez was also disputed by Almagro. Stoddard concludes that physical signs are more often absent than present and that a diagnosis on this basis can only be rarely made, a conclusion which is at variance with our statistics.

The distinctive physical signs (which develop as life proceeds), as well as the absence or late appearance of cyanosis, depend, as Gerhardt pointed out, on the fact that a patent duct of long standing usually has a short, wide lumen through which during systole blood flows freely from the aorta into the pulmonary artery, which dilates accordingly and becomes, with the ductus itself, the chief seat of whatever vibration or murmur the abnormal current may produce; the right ventricle behind it usually undergoes hypertrophy and dilatation as well. Gerhardt described as characteristic a visible systolic pulsation in the second left interspace (indicating the forcible closure of the pulmonary valves), an increased area of cardiac dullness, especially to the right, and a narrow zone of dullness 3 to 4 cm. wide (corresponding, he believed, to the dilated pulmonary artery) lying at the base of the heart, along the left sternal border from the third to the second or first rib, and extending a little way over the first piece of the sternum. This "ribbon-shaped" dullness has been noted by many other observers, and has been strikingly confirmed in a number of cases in which Gerhardt's dull area, with characteristic murmur or thrill localized over it, has been found by the

roentgen-ray to correspond with a pulsating shadow lying above the base of the heart, which was evidently from its size and position the dilated pulmonary artery. In Bittorf's case this shadow was seen, when looked at from the side, to be the size of a walnut and to pulsate a little later than the heart and synchronously with the aorta. In Arnheim's case the roentgen-rays showed, besides enormous hypertrophy of both sides of the heart, which occupied nearly the whole left thorax, the greatly enlarged shadow of the pulmonary artery placed above the cardiac shadow "like a cap," and numerous tortuous dilated vessels, indicating an extensive collateral circulation and a probable coexisting coarctation of the aorta. In the cases reported by Schrötter, Mead, and Hamilton and Abbott, the roentgen-ray cap and Gerhardt's dulness were found at autopsy to correspond with the dilated pulmonary artery.

When cardiac hypertrophy is marked, precordial bulging, diffuse pulsation, and other evidences will be present. An increased area of cardiac dulness, especially to the right, while usual, is not invariable, for the left ventricle may be hypertrophied in excess of the right (Murray's case), or in rare instances there may be no cardiac hypertrophy at all (Drasche's case).

A *thrill*, usually systolic, but sometimes continuous through the cardiac cycle, is fairly frequent, and was present in 23 of the 84 cases; and in 9 of these it was continuous, in 11 systolic and in 3 diastolic. It may be diffuse over the precordium, but is usually localized to the neighborhood of the second left interspace, in the region described as Gerhardt's dull area, or at least is of maximum intensity here. Its transmission obliquely upward below the clavicle (along the course of the pulmonary artery) is said to be pathognomonic.

The auscultatory phenomena are the most important and constant. In infants a harsh systolic murmur with more or less of the above localization is the rule, but in adults a loud murmur is nearly always produced, which is characterized by almost all observers as peculiar, and is variously described as harsh, musical, scraping, scratching, humming, churning, rushing, rolling, and only rarely as blowing. Müller compares it in his case to "rolling thunder," and says that two different listeners likened it independently to the noise made by a train in passing through a tunnel, and Thayer described it in Mead's case as a "machinery murmur." In rhythm several different types may be made out: (1) The murmur is frequently systolic (as in the cases by Murray, Hale White, Simmons, and Bittorf). (2) It may begin with systole, but continue into and through diastole, either as a continuous hum (Chessman's case), or with a systolic rise (Bommer), or with a rhythmic systolic, and diastolic accentuation. Gibson¹ describes as pathognomonic a continuous, rushing murmur which "begins distinctly after the first sound, accompanies the latter part of that sound, occupies the first pause, accompanies the second sound (which may be accentuated in the pulmonary area, or doubled), and finally dies away during the long pause." (3) Sometimes, as in Drasche's case, two independent murmurs

¹ *Medical Press and Circular*, May 30, 1905.

are heard at the pulmonary area, the loud, peculiar, systolic one, and a low, short, diastolic, indicating a slight regurgitation into the aorta during the pause. (4) More rarely the murmur is diastolic in rhythm, as in Fagge's case, in which a diastolic murmur, musical and of a wavy character, was localized to the pulmonary cartilage. The point of maximum intensity is usually in the second or third left interspace, and it is often heard very loudly in the first left interspace below the clavicle and over the first part of the sternum and in the back to the left of the third and fourth dorsal vertebræ, and in the left suprascapular region. In Franck's case and in one by Gillet, the murmur was only heard posteriorly in this situation, and not in front at all. It is transmitted over the left ventricle, and its systolic element often is audible over the carotids, sometimes more distinctly over the left than over the right (Gerhardt). It may diminish abruptly below the third left costal cartilage. In this series of 84 cases, among 20 cases in infants, in 10 a systolic, and in 1 (that by Chessman) a continuous murmur was present. Among the 64 adults, in 13 cases the murmur was systolic, in 13 "double" and in 14 it was the continuous "harsh," "rumbling," "rolling," "churning," "humming" murmur usually with systolic accentuation, described by the earliest students of this subject as characteristic, and which Gibson rightly described as pathognomonic.

Franck mentions, as of diagnostic value, an inspiratory accentuation and an expiratory diminution both of the characteristic murmur and of the radial pulse (*pulsus paradoxus*), which they explain by saying that during respiration the pressure in the thorax is lowered, so that more blood can enter the pulmonary artery than during expiration, and this will lead to a smaller pulse wave from the aorta, to a larger current through the canal, and a correspondingly louder murmur.

The second pulmonary sound is frequently much accentuated, and this is very important as distinguishing patency of the duct from pulmonary stenosis with somewhat similar localization of murmur or thrill. On the other hand, in some cases it may be weak or even inaudible.

In the cases by Schrötter and Mead *paralysis of the left recurrent laryngeal nerve* was present, due to pressure upon the nerve by the enlarged patent duct. Schrötter based a correct diagnosis on this feature. The nerve was degenerated on microscopic examination.

The physical signs are very often obscured by those of other lesions, as malignant endocarditis or arteritis, chronic valvular disease, or other cardiac anomalies so commonly associated. The peculiar character of the murmur, its more or less prolonged rhythm, its localization, and that of the thrill when present, high up toward the left infraclavicular region, with the results of roentgen-ray examination, remain, even in these complicated cases, of the first diagnostic value. Patent duct must be diagnosed also from perforation of the aorta and pulmonary artery just above the semilunar valves, whether of inflammatory or congenital origin. Brocq¹ gives a long series of cases of both types.

So-called Aneurisms of the Ductus Botalli.—This term is used in the literature with a rather irregular application to denote a dilatation in

¹ *Rev. de méd.*, 1886, 6, 786.

whole or in part of a persistently patent duct. That the cases are not aneurisms in the strict sense is inferred by most writers. Rokitsansky uses the qualifying word "so-called." Gruner says that arterial dilatation would often be a better word, as there is usually no change in the vessel wall, and he draws attention to the fact that in the usual bean-shaped form the constriction at either end makes the ductus appear larger to the eye than it really is. Klotz has suggested that, as in his injection experiments the duct is seen to be much larger at birth when distended with fluid than when contracted at the autopsy, many of these small, so-called aneurisms, measuring less than 1 cm. in their greatest diameter, are really not even a dilatation, but are a simple distention of a patent duct to its full capacity by the coagulum within. Again, a further confusion exists in that the term is applied more widely by some writers than by others. Nevertheless, the cases recorded form a fairly well-defined group, which, from their rarity and from the fact that the duct is usually occluded by thrombus, are chiefly of pathological interest, although their occasional rupture, and also the risk of embolism from the thrombus within, increase their clinical significance. The first cases reported were by Billard, Thore, and other French writers; Rokitsansky followed with his monograph in 1852, and Virchow in 1856; full studies of the literature with original cases are to be found in the theses of Westhoff,¹ and Gruner.²

In what may be taken as the classical form (which is that described by Rokitsansky) the ductus forms a spherical or ovoid tumor larger at the middle than at either end, but smallest toward the pulmonary artery, with which, as well as with the aorta, it communicates, filled with old or recent thrombus, and varying in size from a "cherry stone" (Billard) to a "hazel nut" (Thore), or even a walnut (Hebb, Binzer). In Hebb's case,³ in a man aged forty years, an aneurism the size of a small walnut, filled with old clot, lay in the position of the duct, communicating with the aorta by an orifice one-eighth of an inch in diameter, and abutting against the obliterated left pulmonary artery and left bronchus. All the cases recorded are in infants excepting that by Hebb.

In Thoma's⁴ patient, aged twenty-six years, the aorta, from the isthmus downward for about 4 cm., was dilated in the form of a spindle, was lined by atheromatous plaques, and on its right wall opposite the left subclavian artery was a saccular aneurism, in the floor of which lay a small hole representing the lumen of the greatly shortened ductus leading into the pulmonary artery, which was here firmly adherent to the aorta. Microscopic examination showed this aneurism not derived from an expansion of the aortic end of the ductus, but to be a bulging of the aortic wall, which the writer thought was pulled to the right by the action of the contracted ductus. Rokitsansky's 5 cases of funnel-shaped patency were explained by Thoma in the same way, and a special form of "traction aneurism of the infantile aorta" was thus established by him. In Wagoner's 3 cases, aged respectively thirty-eight, forty-two,

¹ *Göttingen Diss.*, 1873, (quoted by Gruner and Voss).

² *Freiberg Diss.* 1904.

³ *Trans. Path. Soc.*, London, 1893, **44**, 45.

⁴ *Virchow's Archiv*, 1890, Bd. 122, p. 535.

and twenty-three years, the duct formed a distinct canal with a small lumen open on the side of the aorta, where the orifice lay in the floor of a hollow in the wall of this vessel, and was sheltered by a distinct fold of aortic intima projecting downward from above while the pulmonary end was closed in by a thin membrane, which bulged into the pulmonary artery. Mycotic aneurism of the patent duct of the dissecting form has been described by Buhl.

Absence of the Ductus.—Absence of the ductus may occur, and is usually associated with hypoplasia and shortening, sometimes with atresia, of the pulmonary artery. It is explained as due to a primary failure of development of the sixth left branchial arch (which persists as the ductus), the stenosis of the pulmonary being secondary. In these cases a septal defect is present, through which the aërated blood passes from the right heart to the aorta.

Anomalous Course.—Multiple origin is reported by Peacock in a case of pulmonary stenosis, two small trunks arising at the site of the normal ductus and passing, the smaller into the left, the larger (which was cut short) apparently into the right pulmonary artery. In several cases the canal has given off the left subclavian. In one case, of right aortic arch, the duct entered the descending aorta below the right subclavian and itself gave off the left subclavian artery.

COARCTATION OF THE AORTA

This term applies to a well-recognized group of cases in which there is a narrowing or stenosis, amounting sometimes to a complete obliteration, of the descending arch at, or immediately below, the so-called isthmus of the aorta, which is that part of this vessel lying between the left subclavian artery and the insertion of the ductus arteriosus. During the period of fetal circulation this segment is comparatively little used, and at birth is usually observed to be of slightly smaller lumen than the adjacent portions of the aorta, the difference soon disappearing under normal conditions. Thérémín states, as a result of his measurements of the normal infant heart, that in 80 per cent. a slight diminution in diameter exists in the isthmus during the first three months of postnatal life, after which a calibre uniform with the remainder of the arch is attained; and that in some 6 per cent. a slight difference remains throughout life which he does not consider abnormal unless it amounts to more than 2 mm. Bonnett classed as anomalous those cases in which the difference was about 3 mm.

Two distinct groups of cases are understood under the term. (a) A diffuse narrowing of the aorta at the isthmus (Bonnet's infantile type). In some of these cases in which the stenosis is marked, the circulation in the lower part of the body is maintained by a large patent ductus arteriosus through which *the descending aorta appears to be a direct continuation of the pulmonary artery*. Such cases, being essentially the same in origin as coarctation, may be included with it. (b) A more or less abrupt con-

striction of the aorta at or near the insertion of the ductus arteriosus (Bonnet's adult type). Here, where coarctation is marked and has lasted some time, the establishment of an extensive collateral circulation frequently completes the picture and lends distinctive features to what is otherwise an obscure lesion.

Relative Frequency.—The figures in the literature are somewhat misleading, for curiously little account is taken of its occurrence by many workers, and therefore the lesser degrees of coarctation are probably often overlooked in the postmortem room, and cases with well-marked vascular changes may escape diagnosis at the bedside. On the other hand, this subject has been so carefully worked over and brought up to date by successive writers, that its statistics are clearer and more accessible than is the case perhaps in any other chapter of congenital cardiac disease. Very probably, therefore, the 237 cases enumerated here are not far from being the full number recorded, whereas the total number of pulmonary stenosis or of septal defect (which anomalies have not been subjected, at least of recent years, to such careful repeated statistical analysis) must be much higher than that given by any author. For this reason Vierordt's statement that coarctation ranks next in frequency to pulmonary stenosis is probably placing the incidence too high. A truer estimate may perhaps be gathered from the fact that among 205 cardiac anomalies recorded in the *Transactions*, there are 22 of stenosis or obliteration of the aorta at the isthmus and 2 of entire absence of the aortic trunk between the left subclavian and the ductus, against 91 of pulmonary stenosis and 165 defects of the interventricular septum.

The first case was reported by Paris in 1789. Craigie collected 10 from the literature in 1841, von Leeuwen 18 in 1850, Rokitsansky 26 in 1852, and Peacock 46 cases in 1866. Barié,¹ in 1885, gave a review of 91 cases, in which he published the series of the above authors, with others from the literature and two personal observations. The fact that 5 of these are without autopsy findings and 3 (Nos. 51 to 53), are apparently omitted from Barié's text, reduces the number of his cases for statistical purposes to 83. Schichhold, in 1897, added 30 to these, and Vierordt, in 1898, brought the number of recorded cases to 126. In 1903, Bonnet² published an article analyzing Barié's findings, and adding to these a synopsis of 77 additional cases which include the series of Schichhold and Vierordt, making, together with the 83 cases collected by Barié, a total of 160, of which 55 are in infants and 105 in adults. In 1915, the writer collected 52 additional cases, making, with Barié's and Bonnet's cases, a total of 212 cases, of which 70 were in newly born and 142 were in subjects over one year of age. Since then additional cases have been recorded, and in 1926, King³ reviewed the subject. From this and other sources 25 new cases have been added to the writer's previous series,

¹ *Révue de médecine*, 1886, 6, 501.

² *Ibid.*, 1903.

³ *Arch. Int. Med.*, 1926, 38, 69.

making a total of 237 cases, of which 82 are of the infantile and 155 of the adult type of coarctation.¹

Pathogenesis.—The proximity of the stenosis to the insertion of the duct in the aorta suggests that the part which this vessel takes in the circulation, or the changes which go on in its form and tissues during its closure after birth, have an essential bearing on the production of coarctation. Rokitansky (1852) assumed *in all cases*, as the essential condition, a persistence of the isthmus and a consequent weakening of its walls so that they yielded, in a way the healthy aorta would not do, to the traction exerted upon them by the contraction of the duct in its obliteration. Skoda (1855), made the interesting suggestion that in those cases in which the isthmus was not obliterated at birth as a true anomaly brought about by an atrophy of the corresponding embryonic aortic arch, the tissue of the duct had extended into the wall of the aorta, which thus contracted as part of the same process by which the canal itself is obliterated, and Brunner (1888) supposed the transplantation of free portions of the ductus tissue into the adjacent wall of the aorta to occur, rather than its direct extension.

Bonnet gave the most satisfactory contribution; he divides the cases of coarctation into two types, according as these occur in the newly born or in adults, for each of which he claims a different etiology:

1. *Infantile Type.*—The form described as that usually seen in the *new-born* is a diffuse narrowing of the isthmus, assumed to be of developmental origin; it is frequently associated with grave anomalies; in it the ductus arteriosus is often patent. The cases in this type fall again into two classes as regards their etiology: (a) When, as in the majority of cases, the stenosis is moderate in degree, it is explained as a persistence of the isthmus at birth, an arrested fetal condition in which this segment fails to attain its normal calibre, and the cause of which is to be sought at or shortly before birth in a simple weakening of the vessel wall, the result probably of a lowered state of general nutrition. Thus

¹ Following are the more important references for the 77 cases, additional to the 160 of those summarized by Barié and Bonnet, studied by the writer: 15 are from a series of 18 cases collected by Fawcett from *Guy's Hospital Reports* and published in 1902; 12 are from the *Transactions* reported by Chevers (1, p. 55), Rees (2, p. 203), Peacock (7, p. 83), Lees (31, p. 58), Wilkes (11, p. 57), Smith (1, p. 52), Barlow (27, p. 41), of coarctation in infants, and by Peacock (12, p. 38), Finlay (30, p. 262), King (23, p. 83), Habershon (39, p. 71) Mackenzie (31, p. 66), in adults.

Other cases are reported by Preisz (*Jahrb. f. Kinderheilk.*, 33, p. 140), Lawrence and Nabarro, Hektoen, Dick (*Proc. Clin. Path. Society*, May 9, 1904), Osler (*Montreal Gen. Hosp. Repts.*, P. M. No. 252), Pansch (*Giessen Thesis*, 1905), Kohl (*Centralbl. f. allgem. Path.*, 1909, 20, 69), Bergman (*Arch. f. Kinderheilk.*, 1919, 67, 44), Fraser (*Proc. N. Y. Path. Soc.*, 1921, 21, 91), Bruce and Ball (*Am. Jour. Med. Child.*, 1921, 31, 196), and Lambert (*Bull. Int. Assn. Med. Mus.*, 1922, 8, 77), in infants, and by Pappenheimer (*Proceedings New York Path. Soc.*, May, 1905, January, 1906, p. 177, October, 1906), Variot, Church, *St. Bartholomew's Hosp. Repts.*, 1865, 1, 177, one in the Museum of Toronto University, Mönckeberg (2 cases) (*Deut. Path. Gesell.*, 1907, 11, 267), Moon (*Lancet*, June 8, 1912), Sella (2 cases) (*Zieg. Beit.*, 1910, 69, 501), Strassner (*Deut. Arch. f. klin. Med.*, 1909, 59, 349), Oberndorfer (*Verh. deu. path. Gesell.*, January, 1910), MacCallum, Lecount (*Proc. Chic. Path. Soc.*, 1913–15, 9, 337), West (*Med. Jour. of Austral.*, 1919, 2, 1925), Follet et Caille (*Arch. d. mal du cœur*, 1921, 14, 207), Leoper et Marchal (*Bull. Soc. méd. d. hôp.*, 1922, 46, 1190), Goldblatt (*Bull. Int. Assn. Med. Mus.*, 1922, 8, 184; Reifstein (*Jour. Am. Med. Assn.*, 1924, 68, 381), Focken (2 cases), (*Ztschr. f. klin. Med.*, 1921, 14, 207), Smith and Hausmann (*Arch. Int. Med.*, 1926, 38, 367) and the unpublished case of W. F. Hamilton and M. E. Abbott.

Thérémin observed that in the case of his so-called normal infant hearts in which the isthmus was abnormally narrowed at birth, there was a history of premature delivery or of general weakness, and, conversely, that in 50 per cent. of infants born before term or weakly, marked narrowing was present. (b) Those rare cases of the infantile type, on the other hand, in which the isthmus is absent or reduced to an atrophic cord, are probably to be explained, as are also the few recorded cases in which there is a complete absence of the aorta between the left subclavian and the entrance of the ductus, as a failure of development in early embryonic life of that part of the fourth left branchial arch which corresponds to the isthmus of the aorta.

In the 6 reported cases¹ collected by the writer, the thin and hypoplastic aorta gave off the three great vessels from the ascending arch and had no connection with the descending arch except in one (Bergman), in which a small fibrous cord ran from the left subclavian artery to the lower part of the arch. This latter was in all the cases a large trunk directly continuous with the pulmonary artery which arose from its normal position in the conus of the right ventricle and supplied the descending arch and thoracic and abdominal aorta with blood through a widely dilated patent ductus arteriosus. These cases present an actual absence of the descending portion of the aortic arch, and as such are analogous with the cases (described below), in which the arch was absent between the left carotid and the left subclavian and the latter trunk was given off from the descending aorta, just where it was continuous with the patent ductus. All these 6 patients died in early infancy except 1 who lived to five and a half years, and all showed a *generalized* cyanosis, in spite of the fact that the head and upper extremities were supplied with arterial blood from the small aorta, while the lower extremities received their large supply of entirely venous blood from the dilated pulmonary artery; this uniform distribution of the cyanosis under these conditions is to be explained by the development of a collateral circulation which would follow the same paths as in coarctation of the adult type, but would here probably be distributed from the arteries of the lower to those of the upper part of the body.

2. Bonnet places in a second class as the *adult type* those cases seen usually after infancy is passed, in which the coarctation consists of a more or less abrupt constriction of the aorta at or near, often a little below, the insertion of the ductus. This condition, which is never seen in the fetus, nor at birth before the closure of the ductus has begun, is, he thinks, not of developmental origin, but is to be explained on Skoda's theory of an extension of the peculiar tissue of the duct into the adjacent wall of the aorta, which thus contracts after birth along with the contraction of the arterial canal. As the malposed tissue is scanty and tends to be of a width corresponding to that of the narrow ductus, its contraction will have the effect of a narrow ligature or cord. These cases differ from those of the infantile type not only in the character of the stenosis, but also in that an extensive collateral circulation, giving rise to marked

¹ By Hicks, Barlow, Dick, Kohl, Fraser, Bergmann.

physical signs, usually develops, while serious anomalies are generally absent, this last fact arguing in favor of its postnatal origin. The ductus arteriosus may remain patent, but is usually obliterated.

Associated Anomalies.—The distinction drawn by Bonnet between two types of cases offers a new and significant suggestion. A statistical analysis, on the basis of this division, of the 237 cases available gives interesting confirmation of this statement, and points to a radical difference in the etiology of the two groups. The following figures include as *minor* anomalies occurring chiefly in the adult type, anomalous semilunar cusps, irregular origin of the vessels from the arch, patency of the foramen ovale or duct, persistent left superior cava; and as *grave* anomalies, septal defects, transposition of the great trunks, congenital stenosis, etc.

ASSOCIATED ANOMALIES IN COARCTATION IN THE NEWLY BORN (82 CASES).

Series.	Absent.	Minor.	Grave.
Barié	0	3	3
Bonnet	13	11	25
This series	2	5	22
Total	15	19	50

IN CASES OVER ONE YEAR ("ADULT TYPE") (155 CASES).

Series.	Absent.	Minor.	Grave.
Barié	57	19	1
Bonnet	15	11	2
This series	14	22	9
Total	86	52	12

Thus among the 82 cases of stenosis in the newly born (dying under one year), in only 15 instances was there no other defect associated; minor defects were present in 19 and in 50 cases grave anomalies co-existed. That is to say, there is frequently associated with the graver cardiac anomalies that form of coarctation which may reasonably be ascribed to a simple arrest of development in later fetal life, and which is due probably to the depressing influence that led to the associated defects, or possibly in some instances to the disturbed circulation that results from the combined anomaly.

On the other hand, among the 155 cases in patients over one year (adult type), other anomalies were absent in 86 instances, minor defects were present in 52, and grave anomalies were associated in only 12 cases; moreover, 7 of these 12 had not the characteristic sharp constriction seen in the great majority of these cases, but were apparently a persistence of the infantile type; for in 3 (Chiari, Houel, MacKenzie) the pulmonary formed the descending aorta through a large patent duct, and the 4 others were in children of two to five years in whom the isthmus was simply diffusely narrowed. Transposition occurred in only 1 (Fawcett), a child aged two years and nine months, with a stenosis apparently of the infantile type. Persistent left superior cava was noted only once (Bonnet).

Equally significant with this rarity of grave anomalies in the adult

type of coarctation, suggestive, too, of some etiological factor as yet unknown, is the frequent association in this type of a certain set of minor defects in the structures connected with the aortic arch, namely, irregularities in the origin of the great vessels, absence of the ductus (3 cases), double ductus (Hammernjk), and especially *anomalies of the aortic cusps*, which last are relatively so common as to seem to place their combination beyond the range of coincidence. Thus the *aortic valve was bicuspid* (in itself a rare anomaly) *in 18 instances*; its segments were increased to four with fusion of two of these in 1 (Fawcett); in 1 instance (Babington) a small supernumerary cusp had formed on the aortic wall above the others; in 3 there was subaortic stenosis, in the form of a membranous band below the cusps, and in 1 there was subaortic stenosis and a band of fibrosis with contraction above the aortic cusps.

In the infantile type, on the other hand, amid so many grave anomalies, bicuspid aortic valves occurred only 3 times.

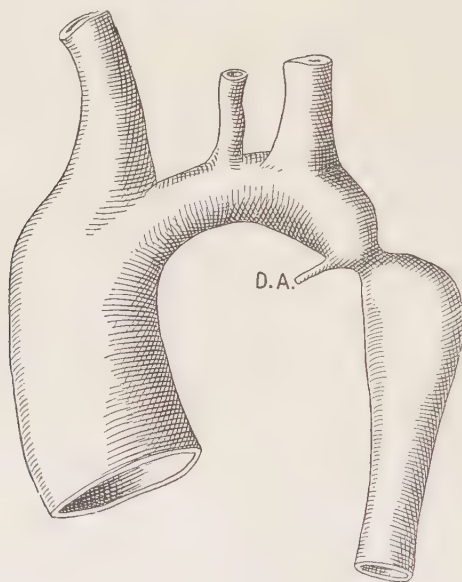
Pathology.—1. The diffuse stenosis of the isthmus usually observed in infancy and always present during the period of the fetal circulation (Klotz), is seen occasionally, but rarely, in later life. It is usually limited below by the ductus, and may begin above as a gradual diminution of the arch, or abruptly at the origin of the left subclavian artery, or, in a few instances, in which the isthmus itself appears to be placed higher up than usual, at the innominate or left carotid artery. The ascending aorta may be dilated or of normal calibre, and below the stenosis the vessel may remain smaller than usual, may return to its full size, or in cases where its descending portion is supplied by a patent duct, be much dilated. The lining of the stenosed area is usually smooth and healthy. In degree it may vary from a mere shade below the normal to a lumen of 1 to 2 mm. in diameter, or be represented in rare instances by a fibrous obliterated cord. Among the total 237 cases, the pulmonary artery formed the descending aorta through a large patent duct in 25 instances, in all of which marked coarctation of the infantile type existed, or (in 6 instances) absence of the arch beyond the left subclavian.

2. *Adult Type.*—A very different anatomical character and a much wider variation are presented. In typical cases the aorta is abruptly constricted at the level of, or a little above, or, most frequently, directly below the insertion of the ductus, as though by a tight ligature or cord, the groove thus formed being usually deepest on the convex side of the arch, which appears deeply indented as though cut through in V-shaped manner (Fig. 90). The aorta on either side usually diminishes rapidly toward the stenosis in an hour-glass or funnel-shaped manner, or it may be dilated on either side, giving a sausage-like effect (Bradley). Viewed from within, the inner surface of the constriction usually presents a projecting ridge or fold corresponding to the zone of constriction without. This may be so marked as to form a distinct septum bridging across the lumen, sometimes obliterating it entirely or leaving a small central circular or triangular lumen, the constriction involving all the coats of the vessel or only its inner ones, the adventitia passing outside of it like a bridge. In other cases the stenosis may occupy a wide area and

appear from without like an annular band. Kriejk describes it in his case as a sort of resistant ring, enclosing the aorta like a cuff parallel to the axis of the vessel, and Mannaberg as a solid segment 0.5 cm. long just below the insertion of the duct. The lumen varies through all grades of stenosis down to one just admitting a bristle. In 28 cases of the 155 it was entirely obliterated, in some instances by a septum or diaphragm formed within, but more frequently by the elongated annular form of constriction.

The aorta may be of normal calibre above and below the stenosis, or it may be slightly narrowed at its origin and dilated for a short distance up. The diminution in calibre not infrequently begins at the innominate or left subclavian artery, and in a certain percentage of cases is

FIG. 90

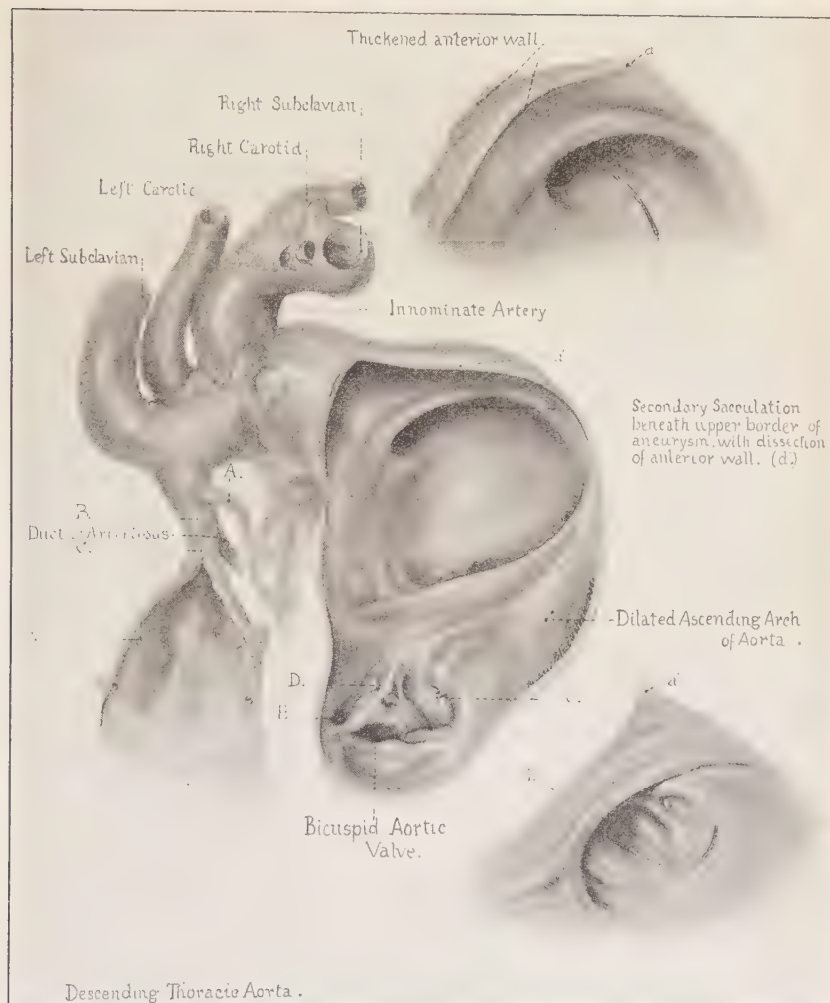


Coarctation of the aorta in a woman aged twenty-seven years. Stenosis beginning just beyond the origin of the innominate artery; sharp constriction immediately below the insertion of the obliterated ductus (D. A.). (Reproduced from Bonnet's article, *Revue de médecine*, 1903.)

followed by a dilatation, below which again the characteristic tight constriction near the duct takes place; the effect being that of a *double stenosis*. The aorta immediately below the stenosis is often widely dilated at the seat of origin of the intercostals. *Hypoplasia* of the vessel in its whole length existed in the cases of Hale White, Riegel and Mönckeberg (2 cases). In other cases the aortic walls, otherwise healthy, are noted as abnormally thin. The aorta may be smooth and healthy in its whole course, as in the cases reported by Brunner (complete obliteration), Cruveilhier, Almagro, Purser, and in the original one by Paris, or there may be extensive atheroma with calcification at the seat of stenosis, above or below it, or throughout the whole aorta. This was present in 42 of the 155 cases, in 9 of which it was definitely stated

to be at the seat of stenosis, in 11 localized in the ascending aorta, in 4 localized below the stenosis, and in 8 diffuse throughout the aorta.

FIG. 91



Coarctation of the aorta with stenosis of the descending arch beyond the origin of the left subclavian, and complete obliteration of its lumen at the point of insertion of the ligamentum arteriosum. Congenitally bicuspid aortic valve with bifid raphé and saccular aneurism of right and posterior walls becoming dissecting at anterior margin. Anomalous artery from descending arch opposite left subclavian (? persistent left fifth arch).

Posterior view showing the descending aorta opened from behind to show the obliterated area, the interior of the aneurism and the secondary sacculaton. *A*, Anomalous artery from descending and to hyperplastic glands; *B*, stenosed descending arch of aorta; *C*, site of coarctation; *D*, raphé behind fused cusp; *E*, dilated left coronary artery, *F*, third intercostal artery; *G*, right coronary arterial (very small). (Case of W. F. Hamilton and M. E. Abbott. Drawing by Miss H. Blackstock.)

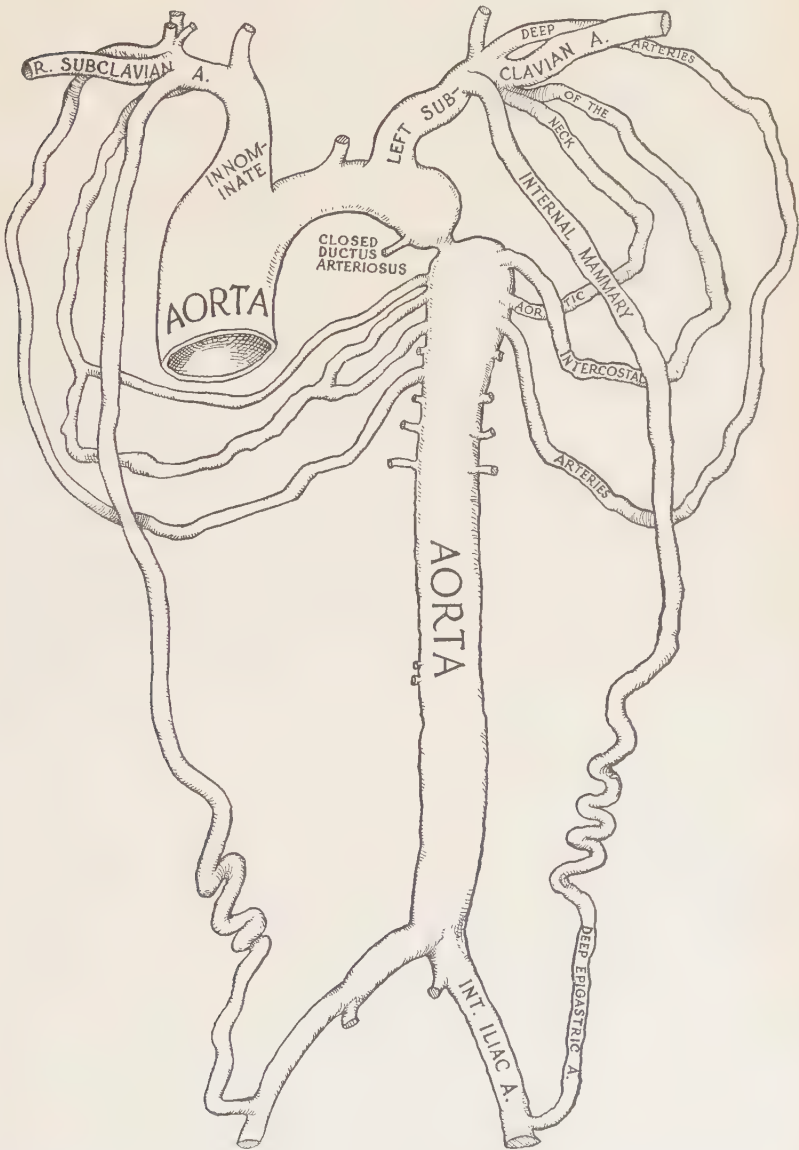
Rupture of the aorta, beginning either as a dissecting aneurism or as a transverse tear, occurred in 18 cases, in 12 of which it lay in the ascending

aorta, a short distance above the valves, and in 6 cases at or near the site of the coarctation in the descending arch. In the case by Sir Astley Cooper the seat of rupture was in the right ventricle of the heart, and in that reported by Laennec (cited by Barié), the right auricle had ruptured into the pericardium. Aneurism of the arch, usually of its ascending portion, but sometimes of the descending arch immediately below the coarctation, is very common and was usually of the dissecting and sometimes of the saccular form. In the writer's case of coarctation figured above (see Fig. 91), a large saccular aneurism of the right posterior aortic wall was undergoing dissection along its anterior border. Sella made a study of 14 cases of rupture of the aorta, which includes two personal observations, and ascribes its frequent occurrence to an abnormal thinning of the ascending arch, which has been noted in a number of cases. Undoubtedly also the association of a bicuspid aortic valve, which was present in about one-half of the cases, militated to the production of the strain which ended in rupture, for this anomaly is in itself sufficient, as was first shown by Babes and Deteindre, to produce a break in continuity of the aortic wall above it, in a large proportion of cases. This combination occurred in Goldblatt's case, a healthy young man, aged eighteen years, with no symptoms except a rather rapid action of the heart. Precordial pain and a sense of enormous intrathoracic pressure with dizziness set in suddenly and he fell unconscious, two days before death. Rupture of the arch was diagnosed on the basis of a large mediastinal shadow pulsating with systole and moving with respiration. At autopsy there was a tear of the inner coats of the aorta on its left anterior wall extending obliquely to the right from a point 1.5 cm. above the aortic ring to 9 cm. above this, forming a dissecting aneurism beneath the adventitia which had ruptured subpleurally and subepicardially as well as into both pericardial and pleural sacs. There was a marked cicatricial contraction of the descending arch at the insertion of the ductus and the aortic valve was congenitally bicuspid and of thin healthy appearance.

In 2 cases (Eppinger, Follet et Caille) death occurred by cerebral hemorrhage induced apparently by the high tension of the upper part of the body. In our case (Fig. 91) death took place eighteen hours after the sudden onset of hemiplegia due either to a cerebral hemorrhage or to an embolus of unknown origin, for the cardiac septa were closed, and the brain not examined. The patient was a boy, aged fourteen years, in whom cardiac symptoms, consisting of periods of precordial pain, dyspnoea and palpitation, had set in with slight cyanosis four years before death. There was precordial bulging and marked pulsation felt with maximum intensity over the base of the heart and along the superficial vessels of the thorax, which were palpable as tortuous pulsating cords, especially in the left axilla and in the interscapular region, as well as a harsh systolic murmur with accompanying thrill, heard all over the chest with maximum intensity over the aortic area but transmitted down along the right sternal border to the apex, and upward into the vessels of the neck and along the dilated collaterals. The roentgen-ray showed a great widening of the aortic shadow to the right and an absence of the pulmonary arc, and the pulse-pressure in the upper part of the body was extremely high (180/40)

while in the lower extremities neither pulse-rate nor systolic pressure could be distinguished, which with the visibly tortuous and dilated collat-

FIG. 92



Diagrammatic outline by W. T. Dawson (after Walsh) showing the course of the collateral circulation in a case of coarctation of the aorta. (M. E. Abbott and W. T. Dawson, *Internat. Clinics*, 1924, 4, 162).

erals, conclusively established the diagnosis. At autopsy, the heart was found to be enormously enlarged chiefly in its left ventricle, and the

ascending arch was ballooned outward to the right and anteriorly as a saccular aneurism the size of an orange with beginning dissection of its wall, which was adherent below and behind to the superior vena cava and right auricle and the aortic valve was bicuspid. The great branches of the arch rose in their normal relation but were displaced far to the left and both subclavian arteries were greatly dilated. The aorta narrowed rapidly at their origin and after the left subclavian became reduced to the calibre of a lead pencil, and 1 cm. below this, at the point of insertion of the obliterated ligamentum arteriosum it was completely occluded. Beyond this point the descending aorta was very narrow but a large collateral circulation had developed between the internal mammaries and the deep epigastrics, and the superior intercostal and dorsalis scapulæ, with the inferior intercostals. This course of the circulation is shown diagrammatically.

In most well-marked cases of coarctation of the adult type the blood supply of the lower part of the body is maintained by the development of an extensive *collateral circulation*. The great vessels of the arch are often enlarged to twice their calibre, and the smaller branches involved are converted into thick, tortuous, dilated trunks. The principal anastomoses are carried on by the superior intercostals, the internal mammaries, and the posterior scapular branches of the transversalis colli *above*, with the first four aortic intercostals, the phrenic and superficial and deep epigastrics *below* the stenosis.

Some evidence of collateral circulation was present in 70 of the 155 cases of the adult type. The particular branches involved and the degree of dilatation vary greatly even in cases of extreme constriction. In 4 instances out of the 155 (Barié, Pic and Bonnamour, Follet et Caille, and Dubreuil) it was expressly stated to be absent; in most of the remainder the collateral circulation was not mentioned, but this does not imply that it was always absent entirely, as minor alterations in the peripheral vessels are easily overlooked.

The *ductus arteriosus* was patent in 15 of the 155 adult cases. In some instances the ligamentum arteriosum is described as "solidified" or much thickened as though by inflammatory action. Among the 85 cases in infants under one year the ductus was patent 63 times.

Marked *hypertrophy with dilatation of the heart* is rare in infants, but occurs in the majority of the older cases, being noted in 97 out of the 155. It is stated by most authors to be the direct result of the obstruction in the course of the descending arch, but the relation of the two conditions is rendered uncertain by the frequent association of chronic valvular disease, which must be a factor in the hypertrophy. Moreover, a few cases are recorded (*e. g.*, Reynaud's aged ninety-two), in which, with marked constriction or, even, as in Brunner's case, an obliteration at the insertion of the duct, the heart has remained normal throughout life. This was stated to be the case in 10 of the 155 cases. This small percentage proves that new channels provided for the blood by the dilated collaterals may be sufficient to carry on the circulation without increasing the work of the heart. In Dumontpallier's patient, aged thirty-nine years, in whom the stenosis was produced by a septum

with triangular central opening, 13 mm. in diameter, and the heart was not hypertrophied, the collateral circulation was carried on chiefly by the aortic intercostals and the vessels from the subclavian, the anastomosis between the internal mammary and the epigastrics being little developed.

On the other hand, an analysis of the 97 cases with hypertrophy shows that while 53 were complicated with chronic valvular lesions or other cardiac defects, in the remaining 44 no cause was present except the coarctation itself. Of the latter, in the 44 cases of hypertrophy without any assignable cause except the coarctation, hypertrophy was confined to the left ventricle in 12, and involved both sides of the heart in 35, of which latter the left ventricle especially was enlarged in 9. An interesting point is that in 27 of the 44, the collateral circulation was either stated to be absent or was not mentioned. These facts argue that even in extreme degrees of constriction the heart may remain normal in the presence of an adequate collateral circulation, but that when this becomes insufficient, cardiac hypertrophy and dilatation supervene.

Age and Sex.—A remarkable predominance of the adult type of the anomaly in the male sex is noted by all writers. Among 146 of the 155 cases over one year, in which this point is mentioned, 102 were in males, and 44 in females.

That the stenosis does not necessarily interfere with the duration of life is proved by the fact that 10 patients died in the sixth and 9 in the seventh decade, while one (Reynaud's) lived to the age of ninety-two years. More than one-half of the remainder (75 cases), died between the ages of twenty and forty years; indicating that, in the anomalous conditions of the circulation that prevail, the system is not, as a rule, equal to the full demands of the stress of normal existence.

In the 155 cases over one year death occurred as follows:

	Cases.
1 to 5 years	7
5 to 10 "	4
10 to 15 "	6
15 to 20 "	24
20 to 30 "	38
30 to 40 "	26
40 to 50 "	18
50 to 60 "	10
60 to 70 "	9
Over 70 "	1
Adults (exact age not mentioned)	12

Incidence of Acute Infective Endarteritis.—An infective endarteritis usually of the subacute bacterial type may occur in the neighborhood of the site of coarctation in the descending arch. In Reifenstein's patient, aged ten and a half years, a mycotic aneurism of pneumococcus origin formed just below the constriction in the descending arch and ruptured into the œsophagus. In Focken's first case, a man aged twenty years with *S. viridans* in the blood stream, the aorta was constricted in cord-like fashion at the insertion of the obliterated ductus, the aortic valve was bicuspid and stenosed with cauliflower-like vegetations on its surface, and at the entrance of the ductus was a narrow cleft leading into a deep

ulceration of the intima surrounded by verrucose and polypoid vegetations. His second case was one of *S. hemolyticus* infection following ulcer of the toe. In Smith and Hausmann's patient, aged seventeen years, who died suddenly in a paroxysm of coughing, a saccular mycotic aneurism 6 cm. in diameter had ruptured into the left chest.

Symptoms and Course.—Coarctation in infants is of little clinical significance, except in so far as it may complicate other grave anomalies. In the adult type it is a condition of the greatest interest and importance. Symptoms when present may be distinguished as those associated with the lesion and those of the cardiac insufficiency which frequently supervenes. As characteristic of the overtaking of the altered circulation, in which the blood supply to the head and upper extremities is freer than that to the lower part of the body, may be mentioned; violent pulsations (Flaherty's case), plethora with sleeplessness and continuous buzzing in the ears (Legrand), violent headaches (Hammernjk), lividity of the face (Chevers, Purser, Kjellberg), suffusion of the head and neck (Moore), epistaxis and hemoptysis (Flint); in Dubreuil's case, a vascular surcharge of the head and chest contrasted with an atony of the subdiaphragmatic viscera; in that of Redenbacher, a boy aged seven years, with a stenosis at the isthmus admitting a crow-quill, and extensive collateral circulation, the development of the head and upper extremities was in advance of that of the lower part of the body. Severe thoracic, epigastric, or abdominal pain and vomiting of long standing (Roemer's case), or pains in the back or lower extremities (Lebert) occur, and may perhaps be due to the local effect of the constipation. Of significance is Muriel's report of a man aged twenty-five years, who was always weakly, and who developed severe pains in the back and symptoms of aneurism of one of the large vessels of the chest; post-mortem a dense mass of enlarged glands the size of a hen's egg was found adherent to the aorta at the point of its constriction; it had eroded the dorsal vertebrae. Precordial pain and oppression, dyspnoea, and severe palpitation may indicate the cardiac strain. Cyanosis is extremely rare except as a terminal event; in only 1 uncomplicated case in the whole series (Almagro), was a true congenital cyanosis present throughout life. Lack of development was noted four times, delayed menses once. Many end with a stage of failing compensation, which, in those not complicated by chronic valvular disease, is usually identical with that of mitral incompetence.

Symptoms are (a) absent, (b) late in developing, or (c) present throughout life. (a) In some of the most well-marked cases of constriction or even obliteration at the isthmus, symptoms are absent throughout life. The condition may be quite latent, and constitute, in Barié's words, a "*surprise d'amphithéâtre*" at the autopsy, death occurring from some intercurrent, independent disease. Thus Crisp describes a chance finding of a stenosis admitting a goose-quill in a soldier aged forty-eight years, who had been in excellent health and had died accidentally, and Scheiber complete obliteration of the descending aorta in a man aged forty-one years, dying of pneumonia, who showed no signs of heart disease. In these latent cases sudden death may occur. In most

instances a rupture of the heart or aorta is found (Lüttich, Barker, Wise, Legg, and others). Death took place without previous warning or symptoms in 19 of the 155 cases.

(b) A large proportion of the cases are in able-bodied, vigorous men, in whom the lesion long remains latent, symptoms developing as the altered circulation becomes overtaxed, or on the intercurrent of some complicating condition, especially endocarditis. Not infrequently, symptoms developing late in life are entirely cardiac in character, cases otherwise latent terminating with a stage of failing compensation which may be due to the lesion itself, or to the chronic valvular disease so often associated.

(c) In a few instances only, symptoms of some obstruction in the cardiovascular system are present throughout life. Quinquaud's patient, a youth aged nineteen years, suffered from infancy with intense palpitation and violent dyspnoea, so that he could not join in play, and œdema of the extremities developed shortly before death, which occurred suddenly. Erman's patient was weakly and had always suffered from dyspnoea. Death took place at 19, after seven and a half months of failing compensation. Lebert's patient, aged twenty-two years, had long had epistaxis and dyspnoea, and developed cardiac symptoms in the last two years.

Physical Signs.—These bear no constant relation to the symptoms, but may be present where these are quite lacking. Nor, on the other hand, do they correspond to the degree of the constriction, nor to the extent of the collateral circulation, both of which may be developed to an extreme degree without yielding any evidence of their presence. The most marked signs appear to be produced in association with chronic valvular disease or bicuspid aortic valves, or with the relative mitral incompetency of the later stages of the cardiac dilatation that frequently supervenes, in which cases the murmurs formed in the heart may be propagated along the vessels. The signs peculiar to the lesion may best be studied in uncomplicated cases. They are both vascular and cardiac, and are present in varying degrees and combinations in the majority of cases.

Vascular.—These depend chiefly upon the inequality of the circulation in the upper and lower halves of the body, and upon the unusual appearances presented by the dilated collaterals. In well-marked cases the vessels of the upper half of the trunk may be seen pulsating, the subclavians, as a rule, more markedly than the carotids; and pulsation may be traced in many cases along the abnormally dilated and tortuous vessels occupying the course of the internal mammaries on either side of the sternum, or the posterior intercostal or scapular arteries behind. In Libman's patient there was a varicose mass beneath the skin of the abdomen; in Flint's, both supraspinous fossæ were occupied by a network of tortuous pulsating vessels; in Leudet's, small arterial dilatations extended over the middle of the thorax both in front and behind, and were most marked at the posterior border of the left axilla and in the left supraspinous fossa, where they formed tortuous, thickened vessels, pulsating synchronously with the radials. Along the whole course of

these a murmur, usually postsystolic in rhythm, but sometimes systolic or double, may be heard, and a slight thrill may be felt.

The radial pulse is frequently hard and full, and may be unequal on the two sides. The lower extremities may contrast strangely with the upper half of the body in the absence of all visible pulsations. On examination the pulse in the abdominal aorta and femorals is either very weak or absent, while the murmur usually audible on pressing over the femoral with the stethoscope cannot be heard. In Bonnet's case, diagnosed before death, no pulse could be felt in the abdominal aorta or femorals, and an artery pulsating visibly and as large as the radial, over which an intense systolic murmur could be heard, ran downward between the vertebral column and the inner border of the left scapula. On the right side of the column a similar but less strong pulsation could be felt, but no murmur was heard.

Hornung's patient, a man aged twenty-seven years, is an example of an extreme stenosis not producing any symptoms, but with marked physical signs, in whom death occurred suddenly from rupture of the aorta. There was energetic pulsation and a systolic murmur over the carotids and subclavians. At the inner border of the scapular region were sinuous pulsating vessels. The radial pulse was hard and resistant, and there was no pulsation in the abdominal aorta, popliteal, posterior tibial, or pedal arteries. As long ago as 1839, Mercier diagnosed a case in which there were visible pulsations in the intercostals, a marked bruit at the lower angle of the left scapula, and a very weak pulse in the lower extremities, with epistaxis and symptoms of failing compensation for three months before death.

Cardiac.—The heart's action may be tumultuous, with a heaving impulse, and the organ may present evidences of enlargement, particularly of the left ventricle. A precordial thrill was present in only 3 of the uncomplicated cases. The heart sounds may be quite pure, or accompanied by loud murmurs, usually systolic or postsystolic in rhythm. In Hornung's patient a rough murmur was heard at the aortic area, most marked between the left clavicle and the third rib. In Decker's, a woman aged nineteen years, with complete obliteration at the isthmus and no complicating valvular disease, a rasping murmur filling the whole systole was heard at the apex, and could also be traced along the thickened, tortuous, and dilated arteries, among which the superior epigastric, the long thoracic, and the dorsalis scapulæ formed pulsating cords; the heart was hypertrophied.

Diagnosis.—When such symptoms and signs as the above occur together a very distinctive clinical picture may be formed. It must be remembered that they may be entirely absent, or present only in a fragmentary way, such as may awaken suspicion of the reality, yet render a positive diagnosis impossible. The fact that physical signs as well as symptoms usually do not remain stationary, but progress to a more definite development, furnishes the clue by which the presence of the anomaly may best be traced. A pulsation at an abnormal area, or a superficial murmur of unusual site, noted and watched, may lead to a second examination, at which the full development of the condition may be revealed.

Even where symptoms are present, the diagnosis may be very difficult between a constriction of the descending aorta at the isthmus and obstruction of this vessel or its branches by aneurism, or by the pressure of a mediastinal tumor. The absence of any considerable area of dulness, the transmission of the murmur for long distances along the branches of the ascending arch, the remarkable extent to which the collateral circulation is sometimes developed, the results of roentgen-ray examination, above all, the difference in blood-pressure in the upper and lower extremities contribute differential points in favor of coarctation. In perhaps no other pathological condition are more extensive changes compatible with fewer evidences during life. The later stage of cases in which vascular phenomena are lacking and failing compensation develops, may be impossible to distinguish from that of organic insufficiency of the mitral valve.

Termination.—The cases may be divided into three groups: (1) The condition may be latent throughout life and not interfere with its duration in any way. (2) Both in latent cases and in those presenting symptoms during life death may occur suddenly, by asystole, from rupture of the heart or aorta, or from causes unknown. (3) Death may follow a stage of broken compensation, which may be preceded by symptoms characteristic of the lesion, or may develop suddenly in an apparently healthy subject; or it may be the result of an infective endarteritis developing at the site of coarctation and running the course of an acute infection.

HYPOPLASIA OF THE AORTA AND ITS BRANCHES

Hypoplasia of the aortic system may be described as that condition in which the lumen of the arterial vessels in the greater circulation remains abnormally small and the walls unnaturally thin and elastic. The heart may also be reduced in size or may undergo a compensatory dilatation and hypertrophy which involves especially the left ventricle, but may extend to the whole organ, and is usually succeeded by a marked degree of secondary dilatation. The subjects are, as a rule, pale individuals of delicate frame, who present signs of retarded development, such as a delayed advent of the signs of puberty. Anomalies of the sexual organs frequently occur. The general health is usually fair until early adolescence, when the condition generally manifests itself after some unusual physical strain has been endured, by the sudden appearance of failing compensation. The course is then progressively downward. In women, who are by natural conditions less exposed to undue muscular exertion than are men, this stage of cardiac insufficiency may not supervene. By some (Ortner, Hiller) the narrowing of the vessels is thought to predispose to the infectious fevers, and a special group of cases in which death has occurred from typhoid fever is described. It is also seen in young anemic subjects dying of pulmonary tuberculosis.

There has been some debate as to the pathological significance of the condition. Several authors have maintained that the greater elasticity of the walls of the vessels compensates for their smaller calibre, and so

prevents undue strain upon the heart. A number of statistical contributions, have, however, demonstrated that hypoplasia of the aorta must be given a place in pathogenesis as one of the special causes of cardiac asystole. The *etiology* is obscure. In some few cases, such as the cachexias of wasting diseases, a true atrophy of the aorta occurs. In the majority some congenital defect, amounting in some instances to a congenital tendency to dwarfism, may be supposed. This view is supported by the frequent association of other anomalies, especially in the generative and circulatory systems. Widely patent foramen ovale and other large defects of the interauricular septum are practically always associated with a true hypoplasia of the aorta, which is possibly secondary to the septal defect, and which dominates the clinical picture. In the presence of a mesocardiac murmur and thrill of congenital origin, the signs of hypoplasia of the aorta constitute an important differential feature, as against defects at the base of the interventricular septum, in which the lumen of the aorta is not usually reduced.¹

Typical cases were described by Morgagni in 1761 and by Meckel in 1788. Rokitansky defined the condition in 1838 and commented upon its association in some instances with defects of the external genitalia. Bamberger, in 1843, noted the association of chlorosis with a small aorta. But in general the subject attracted little attention until Virchow, in 1872, published a series of cases illustrating the frequency of a small elastic aorta and a small heart in chlorosis, and suggested an etiological relation between the two conditions. He explained the absence of compensatory hypertrophy of the heart in some cases and its presence in others, as depending upon the degree of diminution of the lumen of the vessels, the volume of the circulating blood, the elasticity of the vessel wall, and the amount of work done by the individual. Spitzer (1897) attempted to place the condition on a more definite clinical basis. He pointed out that while the cases usually terminate with failing compensation, this resembles the end stages of chronic valvular disease only in a general way, that the symptoms are in general those of a cardiac overstrain due to muscular fatigue, and have a progressive tendency to grow worse; that during the stage of broken compensation the cardiac dulness is usually much enlarged, and that the sounds are generally clear, with marked pulmonary accentuation, although occasionally accompanied by murmurs. Like Virchow, he noted as characteristic a remarkable *pallor*, but he ascribed it not to a diminution of the hemoglobin, which he found usually 90 to 100 per cent., but to the reduction in size of the vessels through which a smaller quantity of blood coursed beneath the skin.

Burke¹ (1901) gave a historical review of the subject and a full account of all the cases on record. He divided the material into four groups:

- (1) Hypoplasia of the aorta in the so-called blood diseases, as chlorosis, pernicious anemia, hemophilia;
- (2) hypoplasia in association with infectious diseases, considered as predisposing to these or tending to their fatal termination;
- (3) hypoplasia with general dystrophies, as acromegaly;
- (4) hypoplasia presenting the picture of a cardiac lesion, the mass of the

¹ *Deutsches Arch. f. klin. Med.*, 1901, No. 71, 187.

cases belonging to this last group. Apelt¹ collected 100 cases from the literature and added an account of 2 cases, both of which were diagnosed during life. The subjects were young men aged seventeen and twenty-one years, of slight build and medium size, who had been capable of the usual amount of physical exertion, and had presented no symptom of disease. Both passed through a period of unusual physical strain just before the sudden onset of symptoms, which took place a few weeks before death. The picture was that of an acute dilatation of the heart with slight terminal cyanosis, œdema, ascites, the cardiac area enormously increased, and the pulmonary second sound markedly accentuated. The heart sounds were pure except toward the close in one patient, in whom a systolic mitral murmur developed. Postmortem, in both cases, the arteries were throughout thin, delicate, elastic, and of diminished calibre, and there was moderate hypertrophy with great pathological dilatation of the heart, although its valves and chordæ tendineæ were delicate, and healthy. Microscopic examination revealed an entire absence of fatty degeneration of the myocardium.

Van Ritoök analyzed 73 cases, 56 from the literature including the series of Burke and Apelt, and 17 from personal observation, and he enumerated the following points as of diagnostic value: (1) The youth of the patient. (2) Marked and obstinate anemia persisting in spite of all treatment. (3) The early development of fatigue in a young individual on slight physical exertion. (4) Subnormal temperature or only slight rise of temperature in febrile diseases. (5) Palpitation. (6) Hypertrophy of the left heart. (7) Acute cardiac insufficiency developing after comparatively slight physical strain. (8) Diminished resistance to infectious diseases.

Bishop² describes what he terms "the congenital type of hypertension" in which high blood-pressure of unknown origin is combined with right-sided preponderance, a narrow aorta and fairly large pulmonary artery as shown by the roentgen-ray, and thinks it important to differentiate this, as the hypertension requires no other treatment but simple avoidance of undue strain. The condition appears to be one of simple hypoplasia of the aorta and transverse position of the heart with or without associated auricular septal defect.

ANOMALIES OF THE AORTIC ARCH

Quite a wide variation of anomalous conditions of the aortic arch and its branches occur, the individual forms of which repeat themselves in different subjects with such similarity, that an underlying developmental error must be inferred. The units of the series may be summed up under the various headings of (1) double aortic arch, (2) right aortic arch, (3) origin of left subclavian artery, from (*a*) a patent ductus arteriosus, or (*b*) the pulmonary artery, (4) origin of the right subclavian artery from the descending thoracic aorta below the left subclavian artery, (5) absence of arch, and (6) common brachiocephalic trunk. In all these

¹ *Deutsches med. Wchnschr.*, 1905, **31**, 1186.

² *Jour. Am. Med. Assn.*, 1923, **80**, 546.

the underlying defect is either a persistence of an embryonic arch which normally undergoes involution (double aortic arch, right aortic arch, left subclavian from patent ductus), or an arrested development of a portion of the embryonic arches that normally persists (right subclavian from thoracic aorta, common brachiocephalic trunk). In man the primitive aorta is at first double and of the six embryonic arches the first, second, and fifth disappear on both sides as well as the left sixth and the distal part of the left fourth, while the third arches persist as the carotid arteries, the fourth left as the aorta, the proximal portion of the right fourth, as the subclavian, and the left sixth becomes the pulmonary artery with the ductus arteriosus.

Double Aortic Arch.—In this, the aorta ascends to the right and turns backward and divides near the beginning of its transverse portion into two large trunks which lie parallel with each other and unite just beyond the insertion of the ductus to form the descending arch, enclosing between them an elliptical space in which the œsophagus and trachea lie embraced. The posterior member of the pair, which is usually the larger, appearing as the true arch of the aorta, gives off the right carotid and subclavian, and lies behind the trachea. The smaller anterior limb lies below the other, appearing like a loop from it, and gives off the left carotid and subclavian, either as a simple trunk (left innominate) or as separate vessels. Examples are recorded by Curnow¹ in a woman, aged eighty-seven years, and by Hamdi,² in a woman aged forty-five years. In the latter case the trachea and œsophagus were slightly compressed. Although no symptoms had been produced, the deformity of the trachea was sufficient to prove the possibility of a fatal obstruction.

Henle explains the posterior limb of the double aorta as a persistence of the fourth right arch. The anterior limb represents the fourth left arch, and the two unite at the point of insertion of the ductus (sixth arch) to form the descending aorta as in the embryo, and as is persistent in the amphibia.

Right Aortic Arch.—In this anomaly the aorta is normal at its origin, but curves over the root of the left instead of the right lung, so that its *convexity* lies to the *left*, and it passes down on the right side of the aorta, the right recurrent laryngeal nerve hooking round the arch in the same manner as does the left under normal conditions. The left carotid, or, in some cases, a left innominate artery, arises from the front of the aorta shortly after its origin and represents the persistent *left aortic root*. The right carotid rises next in about its normal situation, and then the right subclavian more posteriorly and to the right, while the left subclavian arises either (*a*) in its normal situation or (*b*) with the left carotid from the left innominate, or from a patent ductus or from the pulmonary artery.

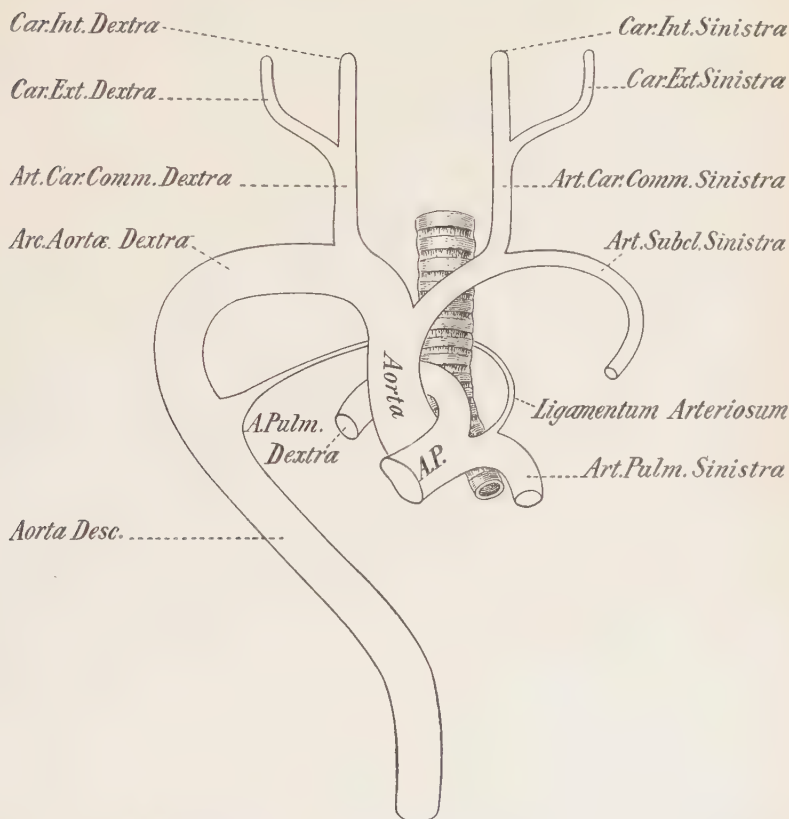
The curve of the aorta passing from the right to left and then back to the right side of the vertebral column becomes very sinuous in those cases in which the ligamentum arteriosus or a patent ductus remains attached to the right aortic arch at its usual site of insertion opposite

¹ *Trans. Path. Soc.*, London, 1874, **26**, 23.

² *Deutsches med. Wchnschr.*, 1906, **32**, 1410.

or near the left subclavian. In these cases the ductus is forced to pass from its origin in the pulmonary artery, on the left side anteriorly, backward and to the right to meet the right arch which curves toward it

FIG. 93



Right aortic arch with ligamentum arteriosum encircling the trachea and œsophagus. Diagrammatic representation following Evans' diagram of the survival of the aortic arches, to show that in the present case the fourth right arch (represented by the arch and trunk of the descending thoracic aorta), the left proximal part of the fourth left arch (represented by the left innominate and subclavian), and the left sixth arch (represented by the ligamentum arteriosum), survive, and that the trachea is necessarily encircled by the passing over of the ductus to the arch of the opposite side. The œsophagus is here omitted for the sake of clearness: (The right subclavian artery which was cut off in the specimen and is not shown, arose from the descending aorta below insertion of the ligamentum arteriosum).

Car. Int. Sinistra, left internal carotid; *Car. Ext. Sinistra*, left external carotid; *Art. Car. Comm. Sinistra*, left common carotid; *Car. Int. Dextra*, right internal carotid; *Car. Ext. Dextra*, right external carotid; *Art. Car. Comm. Dextra*, right common carotid; *Art. Subcl. Sinistra*, left subclavian; *Art. Subcl. Dextra*, right subclavian; *Arc. Aortæ Dextra*, right aortic arch; *Art. Pulm. Sinistra and Dextra*, left and right pulmonary arteries; *D. A.*, funnel-shaped patent aortic end of ductus; *A. P.*, pulmonary artery. (Drawing by J. G. Adams from a specimen in the McGill Museum.)

behind the trachea and œsophagus which are thus again, as in double aortic arch, engaged in a complete vascular circle formed in this case by the aorta, ductus arteriosus (patent or obliterated), and the pul-

monary artery. There are 6 such cases in our series; in 4 of these, all in adults, the ductus was obliterated; in 1 (Garnier¹), a fetus, the ductus was widely patent and with the great vessels formed a vascular arch around the trachea and œsophagus; in the sixth case (Fig. 95), it was widely patent at its aortic end, but was closed beyond, the ligamentum arteriosum forming a long thick cord. In the latter case the aorta gave off a left innominate trunk and then curved backward soon after its origin and to the left, passing behind the trachea and œsophagus and gaining the right side of the vertebral column below. At the point where the convexity of the arch gains the left side of the trachea, it presents a deep triangular pouch, which represents the patent aortic end of the ductus, to the apex of which externally a cord-like structure of remarkable length and thickness, the ligamentum arteriosum is attached. This ligament passes forward anteriorly to the trachea and œsophagus to its attachment in the left branch of the pulmonary artery, and encloses these viscera within the vascular circle formed by it with the aorta and pulmonary artery. In the report by Jex-Blake² of right aortic arch in a pup which was killed in the seventeenth week of its life on account of symptoms of ulceration in the greatly dilated œsophagus, the ductus formed a thick cord 20 mm. long and 0.5 cm. thick which passed from the pulmonary artery on the left side of the œsophagus to the descending aorta at the origin of the left subclavian encircling and constricting this viscus. The trachea was pressed upon by the dilated œsophagus and also slightly constricted by the vascular ring.

Such cases form a link between simple right aortic arch, in which the aorta lies entirely on the right side of the trachea, and double aortic arch in which trachea and œsophagus are completely embraced by a vascular ring. They throw light on the development of the latter, at first sight inexplicable, phenomenon. For, since a right aortic arch must pass behind the trachea to unite with the persistent sixth left arch which is represented by the ductus, it must do the same to unite with persistent left fourth arch which is represented by the anterior limb of the double pair. The whole situation is explained by the reflection that in the embryo these viscera occupy a position, not behind, but on the left posterior aspect of the primitive heart, and that the pairs of embryonic arches pass on either side of them to their destination in the dorsal aorta, so that if arches on opposite sides unite as they have done in the anomalies under consideration, trachea and œsophagus are bound to be encircled.

Right Aortic Arch with Persistent Left Aortic Root.—In right aortic arch the *proximal* part of the fourth left arch usually persists as the left innominate or left subclavian artery and the *distal* part of the fourth left arch disappears entirely. In a few rare instances however, the distal part of the fourth left arch, persists as a diverticulum or abortive branch (*persistent left aortic root*), which passed upward from the descending arch and becomes united to or itself gives off the left subclavian artery. Three cases of this interesting anomaly, diagnosed during life have been reported

¹ *Comptes rend. Soc. biol.*, 1907, **57**, 848.

² *Lancet*, London, 1926, ii, 542.

by Arkin.¹ In one case confirmed by autopsy the patient was a man aged fifty years, who died of a generalized periarteritis nodosa. The roentgenograph showed a broad slightly convex shadow with definite systolic pulsation lying to the right of the sternum and *reaching as high as the right sterno-clavicular articulation* and which passed over into a very narrow convex shadow to the right of the sternum; (2) in the first oblique diameter *the trachea and œsophagus were seen lying anteriorly to the aortic arc*, and the latter viscus (filled with barium) was seen pushed to the left and somewhat constricted with a systolic pulsation of its posterior wall (which lay against the aorta); (3) enclosed within the aortic arc was a *round shadow lying behind the bifurcation of the trachea*, which was recognized as the persistent left aortic root. At autopsy a right aortic arch was found, the curve of which lay in the angle between the trachea and right bronchus and then sloped gently downward behind the œsophagus which was pushed to the left and forward. In the beginning of the descending aorta a diverticulum 1.8 x 1.5 cm. in size was given off from the anterior wall of the descending part which bulged into the left posterior wall of the œsophagus and gave off from its blind end two obliterated vessels, one of which was attached to the left subclavian artery (representing the rest of the fourth left arch), and the other, the ductus Botalli, to the left branch of the pulmonary artery. The right aortic arch itself, gave off first a left innominate and then the right carotid and the right subclavian.

Left Subclavian from Ductus Arteriosus or Pulmonary Artery.—

While the left subclavian is given off from the fourth right aortic arch, it is practically a continuation of the distal part of the sixth left arch represented by the ductus arteriosus to which its origin bears a constant relation, and its origin from this vessel or from the left pulmonary artery represents a persistence of this earlier association. Cases are reported by Holtz, and by Combes and Christopher.²

Absence of Part of Aortic Arch.—Complete disappearance of a part of the aortic arch may happen in one of two situations: (a) In the descending arch between the left subclavian and the entrance of the ductus arteriosus, which vessel in this case remains widely patent and carries the blood from the pulmonary artery to the descending aorta; this is an extreme form of the infantile type of coarctation, and has been discussed in that connection. (b) In the other and much rarer type, and that which concerns us here, the arch is interrupted just after the left carotid and before the origin of the left subclavian, which vessel is given off in these cases from the descending arch of the aorta and the latter vessel has no connection with the transverse arch, but is continuous with the pulmonary artery through the widely dilated ductus. Two such cases are reported (Greig, '1852,³ Hayashi, Goedel. and H. A. Harris).

Right Subclavian from Descending Thoracic Aorta.—In this anomaly the aortic arch has its normal course to the left, but the right subclavian is given off from a point in the thoracic aorta just below the insertion of the ductus arteriosus and passes up to its normal distribution.

¹ *Wien. Arch. f. inn. Med.*, 1926, **12**, 285.

² *St. Bartholomew's Hosp. Reps.*, 1884, **20**, 273.

³ *Jour. Anat. and Phys.*, 1922, **57**, 95.

Here an arrest of the proximal part of the fourth right arch which normally forms the right subclavian has occurred, and the obliteration of the distal portion which in the embryo unites the fourth arch with the aortic trunk has not taken place, and this has persisted as the right subclavian. In its passage to the right side the artery passes behind or between the trachea and œsophagus, or (in rare cases) it may lie in front of them. These relations may lead to dysphagia, especially when the artery is the seat of aneurismal dilatation, and death has occurred from inability to swallow and from rupture of the anomalous artery after swallowing food. The close proximity to the thoracic duct is also of interest and in one patient, death resulted from slow starvation. Erosion of the vertebral column may also occur. The subject was reviewed by Goldbloom¹ (1922), who presents an excellent study with a description of 1 of 4 cases which occurred among 225 cadavers in the dissecting room at the Jefferson Medical College.

Common Brachiocephalic Trunk.—All four great vessels may arise by common origin, recalling the embryonic stage in which all the arches emerged together from the third carotid arch. A case is cited by Freyberger.²

Clinical Aspects.—The evidence presented during life of all the above conditions is usually slight, but a knowledge of the anatomical possibilities with careful examination of available data may yield a correct diagnosis, as in Arkin's cases. In right aortic arch and in common brachiocephalic trunk the high situation of the vessel may lead to an abnormal pulsation in the episternal notch, and in 2 of his cases the aortic second sound was heard best over the right sterno-clavicular articulation. In a case reported by Bard of anomalous origin of the innominate and left carotid from a common sacculation divided internally by a sharp groove, there was a soft but absolutely constant systolic murmur with maximum intensity at the upper left sternal border and transmitted into the neck but not to the apex. The tendency to "*dysphagia lusoria*" in both double and right aortic arch, as well as in abnormal origin of the right subclavian, should always lead to a careful roentgen-ray examination and to the consideration of the possibilities of strangulation by a ligamentum arteriosum, which is susceptible of operative interference. In the case of origin of the left subclavian from the ductus or pulmonary artery, the left arm may remain free from cyanosis, as in Breschet's case, doubtless because oxygen unsaturation does not rise above its threshold value in the absence of obstruction in the capillaries.

ANOMALIES OF THE CORONARY ARTERIES

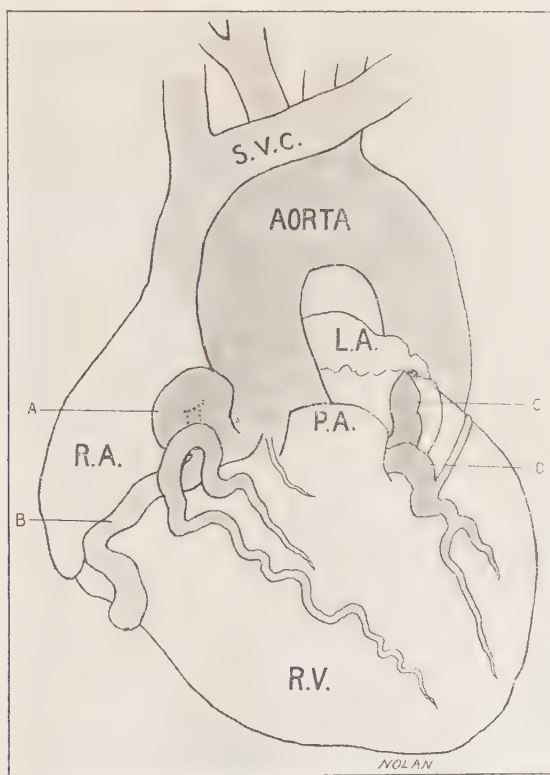
Anomalous Origin from the Pulmonary Artery.—A vessel may arise from a sinus of Valsalva of the pulmonary artery, and, meeting the branches from the aortic coronaries, produce a remarkable anastomosis of a cirroid character. In Brook's first case, a vessel the size of a crow-quill sprang from the right anterior sinus of Valsalva of the pulmonary

¹ Surg., Gynec. and Obst., 1922, **34**, 378.

² *Trans. Path. Soc.*, London, 1898, **44**, 44.

and passed down over the infundibulum of the right ventricle, there anastomosing with the aortic coronaries. In his second case a large anomalous artery arose from the same situation. It gave no branches to the heart but passed to the left and upward to enter a complicated mass of thin-walled arteries, which lay around the main pulmonary trunk and passed up along the trachea and behind the aortic arch. This mass received three other large vessels, one from the left subclavian, one from the right aortic coronary, and one from the posterior aspect of the transverse aortic arch. Krause's case is similar.

FIG. 94



Aneurismal dilatation (arterio-venous aneurism) of branches of coronary arteries in a case of anomalous origin of the left coronary from the pulmonary artery. (From a specimen in the Medical Museum of McGill University, Montreal.)

The McGill specimen (see Fig. 94), was from a woman aged sixty years, who died accidentally. The right coronary arose in its normal situation from the anterior sinus of Valsalva of the aorta by a much dilated orifice, and expanded directly after its origin into a huge thick-walled loop the size of a crab-apple, which projected upward some 2.5 cm. above the subepicardial fat, and gave off the descending branches from the loop. Both these and the main trunk of the vessel were wide, thick-walled, tortuous channels. No coronary arose behind the left

posterior aortic cusp in the normal situation of the left coronary, but instead a large patulous opening lay in the floor of the dilated posterior sinus of Valsalva of the pulmonary artery. From this sprang a large thin-walled trunk of venous character, which divided about 1 cm. beyond its origin into two large branches, one of which ran to the left in the auriculoventricular groove in the course normally followed by the transverse circumflex branch of the left coronary artery, while the other ran downward along the front of the interventricular septum in the position of its descending branch, and was here expanded into a large triangularly shaped venous sinus, 2 cm. in its widest diameter, and diminishing in size toward the apex. In the floor of this sinus were several thick-walled septa behind which large vessels opened into it from the myocardium, strongly suggesting that the course of the blood was *toward* the pulmonary artery.

The question of the circulation in the anastomosing vessels, in which blood from the systemic and pulmonary circulations must have mingled is of interest. Brooks suggests that the direction of the current must have been *toward* the cirroid aneurism in the coronaries arising from the aorta, and toward the right ventricle in the coronary that arose from the pulmonary artery, which would thus drain the mass and would also send some arterial blood to the lungs. The left coronary is always the one displaced to the pulmonary artery, probably due to the anatomical relations of the two great trunks which stand at an angle with each other which has its apex on the left side (Kryokawa), so that if the left coronary is displaced a little forward before the aortic septum is complete it will come to lie on the pulmonary side of the septum.

Both the McGill case and Brooks' second one were in elderly subjects, and the condition had not produced any manifestations during life.

Association of Anomalous Origin of Left Coronary with Congenital "Idiopathic" Hypertrophy.—An interesting series of cases of cardiac enlargement of unknown etiology, termed by the late Dr. John Howland "Idiopathic Hypertrophy of the Heart" has been found to be associated with an anomalous origin left coronary to the pulmonary trunk. This combination has been reported by Abrikossoff (1911), Heitzmann¹ (1916), Kryokawa² (1923), and Carrington and Krumbhaar³ (1924). In all the cases congenital hypertrophy was the predominant feature and presented the characteristic clinical picture of this condition; the myocardium of the left ventricle, that is of the area supplied by the malposed artery was extensively fibrosed and degenerated as a result doubtless of the deficient aëration of the blood transmitted to its walls from the pulmonary artery. In Dr. Stephenson's unreported case, an infant, aged three months, the excessive hypertrophy and dilatation of the left chambers produced atelectasis of the lung, hoarseness, and difficulty in passing the feeding tube from pressure upon the left bronchus, recurrent laryngeal nerve, and œsophagus respectively.

Anomalous Right Coronary.—Two cases are on record in which the right coronary artery pursued an anomalous course with multiple aneu-

¹ *Virchow's Arch.*, 1916, **123**, 57.

² *Deutsche Arch. f. Klin. Med.*, 1923, **242**, 14.

³ *Am. Jour. Dis. Child.*, 1924, **27**, 449.

rismal dilatation while the left coronary was apparently normal. One of these is an unpublished case from St. George's Hospital (personal communication, H. Ingleby). A similar condition is described by Wilson and Grant in a patient with congenital heart block. A small rounded firm nodule about 6 mm. in diameter situated on the upper aspect of the right ventricle under the right auricular appendix proved to be an aneurism of the right coronary artery which opened directly into blood-filled spaces in the myocardium and these in turn opened into the right ventricle behind the lateral flap of the tricuspid valve.

Miscellaneous Anomalies.—Accessory coronaries may be present or both vessels may arise behind a single aortic cusp, or there may be a complete absence of one. A case has been recorded of an anomalous coronary sent to the lungs in pulmonary atresia.

ANOMALIES OF THE PULMONARY ARTERIES

Accessory Pulmonary Artery.—A series of 10 cases has been collected from the literature by McCotter,¹ in which an anomalous artery had arisen from the aorta or its branches, and had supplied the lower lobe or the accessory lobe of one or other lung. In the case reported by himself, in a man aged sixty-five years, this artery was 7 mm. in diameter, and was given off from the front of the thoracic aorta on a level with the tenth dorsal vertebra, and passed up to the right between the folds of the ligamentum latum pulmonis to the lower margin of the right lung, where it ramified. The lung pleura and mediastinum were otherwise normal. In 8 of the cases collected the accessory branch was from the thoracic aorta, in one from the abdominal aorta, and in one from the seventh intercostal artery. In 5 cases the accessory branches supplied an accessory lobe and in 5 the lung was normal.

Pathogenesis.—The final explanation must be deferred until the origin of the pulmonary circulation is better understood. McCotter gives an interesting discussion. Accessory pulmonary arteries have been described in amphibia and reptiles, and are said to be normal in the latter. Thoma and Evans found that the blood vascular system in the embryo arises as a capillary plexus spreading in all directions. Such a capillary plexus forms caudally from the pulmonary arches and envelops the primitive lung *anlage* with a rich capillary plexus. In the case of the accessory pulmonary branch, this plexus must have formed laterally from a primitive thoracic aorta and joined the pulmonary plexus just as a capillary network extends to the limb-bud. The explanation of this anomaly is thus either (1) that this plexus always occurs but has failed to atrophy in the present case; or (2) that the plexus is only occasionally laid down, *i. e.*, is in itself an anomaly, and when present results in an accessory pulmonary branch. The condition has not shown itself to be of any clinical significance.

Cystangioma of Pulmonary Wall.—A remarkable condition was described by Barbacci,² in which a pedunculated elastic body the size of

¹ *Anal. Rec.*, August, 1910, 291.

² *Arch. Sci. Med.*, 1890, 15, 1.

a pea was attached to the wall of the pulmonary artery directly opposite the corpus Arantii of the anterior cusp a little below its free margin. It contained a cystic cavity filled with blood and divided into secondary cavities by trabeculae and had a lamellated wall identical with that of the arterial media and communicated by an oval aperture with the axis of the pulmonary artery. The author thought that the cyst and tubular dilatation of the wall might represent the remains of the right aortic arch which was here incompletely obliterated and later retained an accidental connection with the artery. A pedunculated tumor in this situation was noted also by Cruickshank.

ANOMALIES OF THE SYSTEMIC VEINS ENTERING THE HEART AND OF THE PULMONARY VEINS

Systemic Veins.—*Persistent left superior vena cava* is the commonest of these anomalies. It is not infrequent in conjunction with other cardiac defects, and occurred 28 times in our series. It is of little clinical importance but is of great interest in cases where the congenital origin of the associated condition is questioned, as indicating the developmental nature of the latter. The cases may be divided into two groups: those in which the right superior cava is also present, and those in which it is absent, and the blood from the upper portion of the body enters the right auricle through the persistent left cava. A series of 4 cases of persistent left cava is published by Schutz.¹ In three of these the right cava was also present, in one it was equal in size to the left; in a second it was small and the left cava communicated with the left auricle by a valvular opening in its wall before entering the right auricle at the coronary sinus. In this case the apex of the heart was bifid, and the patient was a woman of thirty-eight of whom no other history was obtainable. In the third case the left superior cava was persistent but rudimentary. In Schutz's fourth case the *right superior cava was absent*. The right innominate veins emptied into the left innominate at the level of the left common carotid to form a left superior cava thicker than a man's thumb which widened into a bulbar swelling 4.5 cm. across, which entered the coronary sulcus and opened into the right auricle above the inferior vena cava. Habershon² reported a case of absence of the superior cava in a man aged thirty-seven years. The usual opening of the superior cava in the right auricle was marked by a smooth, white area of endocardium, like a closed foramen ovale, and there was extensive development of collateral circulation through the vena azygos major. The persistent left cava was formed by a union of the left jugular and subclavian and right innominate veins and emptied into the dilated coronary sinus. The literature on complete absence of the right superior cava with persistent left is given by Dietrich.³

A very interesting case is published by Beyerlein,⁴ in a boy, aged one and a quarter years, of double superior vena cava, in which the orifice of the coronary sinus in the right auricle was obliterated by the over-

¹ *Virchow's Arch.*, 1914, **216**, 35.

² *Trans. Path. Soc.*, London, 1876, **127**, 79.

³ *Virchow's Arch.*, 1913, vol. **212**.

⁴ *Frank, Ztschr. f. Path.*, 1914, **15**, 327.

growth of an extensive network of Chiari. The persistent left cava received all the blood from the coronary veins and the heart, and emerged from the coronary sulcus at the normal situation, emptying into the right superior cava through the transverse branch. Two cases practically identical with this very rare anomaly are reported by Gruber¹ and LeCat (quoted by Gruber). Nabarro² describes a case of double superior cava in an infant of three months where the persistent left duct, smaller than the right, was joined by the left hepatic vein, which emptied with it into the coronary sinus. Here the left horn of the embryonic sinus venosus had evidently escaped obliteration.

A series of cases in which a *displacement to the left* of the superior cava has taken place so that its orifice comes to lie directly above the interauricular septum, and looks into both auricles, which has been described by Ingalls and others, and a similar condition of the inferior cava by Rokitansky, are described under auricular septal defects.

Pulmonary Veins.—An anomalous distribution of the pulmonary veins is much more common than is generally supposed, and quite serious deviations from the normal have been attended with surprisingly little results. Nevertheless, their displacement occurs in many complicated anomalies, and their repeated combination with these grave defects suggests a primary error in development in the pulmonary veins *anlage*. Quite a large series of cases of biloculate heart are reported in which the pulmonary veins were deflected from their entrance to the left auricle and were received by one or other of the great veins. Schroeder³ gives a full discussion of the various anomalies of the pulmonary and systemic veins and traces their developmental origin, with especial reference to those cases, like his own, in which a complete defect of the interauricular septum was associated. Nabarro describes the pulmonary veins opening into the coronary sinus in an infant aged five and a half months, in whom all the blood from the systemic circulation must have passed through the patent foramen ovale.

In the cases reported by Ingalls,⁴ Chiari and others, of defects at the upper part of the interauricular septum, the right pulmonary veins either entered the right auricle or the superior vena cava. In those reported by Borst and Stoeber⁵ of an anomalous septum in the left auricle, the pulmonary veins entered the smaller upper chamber in the left auricle to the right of the anomalous septum, which evidently represented the septum primum, deflected to the left by the entrance of the pulmonary veins too far to the right side. In all, the primary defect is apparently the deflection of the pulmonary veins.

Ramsbotham describes a case in which the left pulmonary entered the left subclavian, and the right pulmonary the portal vein, and in three others (Arnold, Bochdalek, Geipel) the right and left pulmonaries entered the portal vein together as a common trunk. The pulmonary veins of both sides may enter the left auricle as a single or as two trunks.

¹ *Virchow's Arch.*, 1885, **99**, 492.

² *Jour. Anat. and Path.*, 1902, **37**, 387.

³ *Arch. fur. klin. Med.*, 1911, **205**, 122.

⁴ *Johns Hopkins Hosp. Bull.*, 1907, **18**, 136.

⁵ *Virchow's Arch.*, 1908, **193**, 252.

Here the original single vein has not been taken up in the wall of the auricle as occurs in normal development.

The *clinical significance* of these conditions depends less upon the defect itself than upon the associated developmental conditions.

CONGENITAL ARTERIO-VEINOUS FISTULA

The clinical features of arterio-venous aneurism were first described by William Hunter in 1757, but it was not until 1867 that a case presumably of *congenital* origin, was reported by Sir Prescott Hewitt. Since then some 20 cases, supposedly of congenital origin have been recorded of which only 5, those by Eiselberg (1899), Halsted (1918), and 3 cases reported by Rienhoff,¹ have definite proof, by dissection at operation or autopsy, of the nature of the anastomosis. These statements are quoted from the study by the last author, who has shown (1) by experimental evidence (Sabin), that anomalous communications with an arterio-venous shunt of the blood flow through these, may and do readily develop in the vascular network of the early embryo as a direct result of intra-uterine trauma or infection; (2) also that such communications may remain latent or potential during the early years of life, opening as actual passages for an arterial-venous flow at or after puberty; and (3) that such an arterial-venous fistula of congenital origin presents all the *local appearances* and produces the same *remote effects* upon the circulation as does the acquired form, except that the hypertrophy and dilatation of the heart, known to be a constant feature of acquired arterial venous aneurism, has been invariably absent in the congenital cases observed. Since Rienhoff's article Reid² and Bernheim³ have added 2 cases making 22 cases in the literature, of which only the 5 enumerated have been definitely proved.

Pathological Anatomy.—In arterio-venous fistula the communication is between arteries and veins of the second or third grade, and the resulting changes in the parts affected are (as in acquired fistulous openings): (1) Enormous dilatation of that part of the artery proximal to, and reduction in that part distal to, the fistula; (2) marked proximal and distal dilatation of the veins with degenerative changes; (3) infiltration and œdema of the parts distal to the fistula with evidences of increased growth, both in girth and length of the extremity. The absence of hypertrophy of the heart in all the congenital cases suggests that the slow development of the circulatory disturbance in the congenital cases is the cause of this and that some other reason for the cardiac enlargement that occurs in all cases of acquired arterio-venous aneurism and in most cases of coarctation of the aorta must be supposed (Rienhoff). The size of the fistulæ in these 5 cases varied from 0.25 to 3 cm. in diameter, and the anastomosis was lateral in 1, end-to-end in 2, and intermediate in type in 2 cases.

Clinical Aspects.—A congenital arterio-venous fistula usually first manifests itself as an indefinite pulsation or small hard swelling in the region of the popliteal, brachial, tibial, femoral, carotid or other medium-sized artery, which may develop spontaneously or as a result of trauma,

¹ *Johns Hopkins Hosp. Bull.*, 1924, **35**, 271.

² *Arch. of Surg.*, 1925, **40**, 25; **41**, 601-996.

³ *Ann. of Surg.*, 1925, **81**, 465.

and which gradually reveals its nature by the appearance of an expansile pulsation and peculiar buzzing or machinery hum with accompanying systolic or continuous thrill. Marked increase in size of the affected limb is common, especially when the lesion has manifested itself in childhood or early infancy, and diffuse pulsation, turgescence or varicosity of the veins of the affected side with reduction in volume and lowered systolic pressure of the arterial pulse beyond the lesion follow. Attacks of cramping pain and persistent incurable ulcers are common and in one case there was gangrene of the great toe. When the anastomosis is lateral by multiple small arterial twigs, as appears to be in the case in the majority of instances, conditions are favorable, for the local signs of a stream passing through a relatively small opening are liable to be pronounced, making the diagnosis clear, while the stage of adjustment, in which the patient's general condition is otherwise good, is correspondingly prolonged, and operative interference by dissection and ligature of the involved vessels (where these are accessible) has been successful in a number of cases.

The *remote effects* upon the circulation of an arterio-venous aneurism, as described by Lewis and Drury¹ are seen in a well-developed congenital arterio-venous fistula in the stage of adjustment. These are, briefly, increased heart action, lowered diastolic pressure (raised pulse-pressure), difference in arm and leg systolic pressures (Hill's sign), a soft apical systolic murmur transmitted up above the left sternal border and not to the axilla (which is always present in a peripheral vascular leak and does not indicate cardiac insufficiency) as well as the phenomenon described by Matas² as "Branham's bradycardiac reaction," in which closure of the fistula by digital pressure results in a marked slowing of the pulse, raised diastolic pressure, disappearance of the cardiac murmur, and (in the acquired cases), diminution of the heart's area as seen by the roentgen-ray. Slight dyspnœa or hyperpnœa, a tendency to pallor of the surface, and an under-developed state of the individual, are also significant features. The actual absence of cardiac hypertrophy during the stage of adjustment in all the cases recorded to date appears to be due to the slow development of a congenital lesion and should be of diagnostic value. This feature is also important as supporting the findings of Lewis and Drury that the peripheral venous pressure is *not* increased in arterio-venous aneurism and that cardiac dilatation and hypertrophy when existing in these cases are *not* due to an increased venous return.

If the fistula is not relieved by operation, the strain upon the circulation will in time pass the borders of compensation, and the cardiac insufficiency that results will reveal itself by a jerking and capillary pulse, arrhythmia, dyspnœa, functional incapacity and finally by the signs of severe decompensation. An important feature at this time is the disappearance of the "bradycardiac reaction," the diastolic pressure remaining low and the pulse-rate raised, in spite of closure of the fistula, and this is a sign of prognostic as well as diagnostic value.

Rienhoff's patient, a man, aged twenty years, presented a pulsating rumbling mass with a marked thrill and loud to-and-fro machinery murmur over the left side of the neck, immediately below the left ear, which had been present ever since he could remember. Beyond a slight short-windedness

¹ *Heart*, 1923, 10, 306.

² *Internat. Clinics*, 1925, 2, 58.

on exertion there were no cardiac symptoms and the electrocardiogram and roentgenogram of the heart were normal. Pressure over the point of maximum intensity of murmur and thrill, just below the angle of the left jaw, caused complete collapse of the tumor and disappearance of the signs over it, due to obliteration of the venous supply to the fistula. The left retina was redder than the right and the left retinal veins were much larger and more tortuous, while the retinal arteries were smaller on this side. The pulsation of the tumor extended both into the mouth and upward, so that the left tonsil as well as the lobe of the left ear pulsated synchronously with each systole of the heart and there was marked flushing of the left side of the face and diplopia. Operation was carried out with very careful dissection of the parts, and revealed an enormously dilated pulsating venous external jugular vein 4 cm. in diameter, which contained mixed venous and arterial blood, and between which and the external carotid artery 8 fistulous communications were dissected, 3 on the posterior and 5 on the anterior aspect of the vein. All these branches were ligated and the patient made an uneventful recovery. This is the first case in the literature of a congenital arterio-venous aneurism having been successfully operated upon and cured by operation, and the only one in which multiple fistulous communications (mirroring the embryonic origin of the anomaly) have been demonstrated by actual dissection and exposure at operation.

Congenital Hemangiomata.—These are masses of telangiectatic capillaries derived from the same type of embryonic anastomoses as congenital arterio-venous fistula, and they are sometimes associated, as in 2 of the cases collected by Rienhoff, those by J. C. Warren (1846) and by S. W. Gross (1867). They are sometimes associated with anomalies of the vessels from the aortic arch as in an infant some five months old with multiple hemangiomata of the face and neck reported by Eder¹ who at autopsy had a patent ductus and a right aortic arch; and in the case by Ghon of left subclavian from the pulmonary artery, the left lung was the seat of extensive hemangiomata. Marked enlargement of the left arm in proportion to the rest of body in a patient aged thirty-five years, was reported by Wakefield,² and over the back of the hand and extensor surfaces of arm and forearm over the shoulder and pectoral fold, was an extensive superficial angioma of sinuous outline, which blanched completely on pressure. The veins on the left arm were more prominent than the right and were slightly varicose. The heart was not hypertrophied and there were no murmurs. The blood-pressure was 110/70 and equal in both arms.

PART III

DIAGNOSIS, PROGNOSIS, AND TREATMENT

DIAGNOSIS AND PROGNOSIS OF CONGENITAL CARDIAC DISEASES

Differential Diagnosis.—This subject has been discussed in most cases under the different defects, but certain general statements are in place

¹ *Deutsches Med. Wchnschr.*, 1908, No. 26; 1909, No. 28, p. 1252.

² *Am. Jour. Med. Sci.*, 1926, 171, 569.

here. In the diagnosis two questions are to be considered: a congenital is to be distinguished from an acquired lesion, and the differentiation is to be attempted of the particular defect. It is necessary, in the first place, to recognize the congenital nature of the lesion, and this can usually readily be done. The following conditions are significant of the presence of a defect: (a) The youth of the patient. (b) A history of symptoms originating in early childhood or in infancy, and of the absence of any event, as rheumatism or endocarditis, which could have led to an acquired lesion. (c) The cyanosis when this is present, and the symptom complex associated with it. (d) The presence of atypical physical signs.

The diagnosis of the various defects from each other is a more difficult task. In some of the most complicated forms of congenital cardiac disease both signs and symptoms may be conspicuous by their absence. And on the other hand, several anomalies are frequently combined in the same case, so that a bizarre picture is liable to be produced, even in the presence of marked and characteristic physical signs. Nevertheless, careful study of this subject has convinced the writer that, in the great majority of cases, auricular and ventricular septal defects, abnormal communication between the aorta and pulmonary artery, patent ductus arteriosus, subaortic stenosis, and coarctation of the aorta, all of which conditions are characterized by *slight* or *absent cyanosis*, can be distinguished from each other and from those graver cases of pulmonary stenosis or atresia, biloculate and triloculate heart, persistent truncus arteriosus and transposition of the arterial trunks, *in which cyanosis is a conspicuous feature*.

Cyanosis is the rule in pulmonary stenosis and atresia, in complete defects of the septa, as biloculate or triloculate heart or persistent truncus arteriosus, and in transposition of the arterial trunks, in all of which oxygen-unsaturation of the blood is raised above the threshold value at which cyanosis appears, usually by the direct entrance of venous into arterial blood from right to left through the defect (Lundsgaard's *alpha factor*), or by an increased deoxygenation in the capillaries (as in the rare cases of pulmonary stenosis with closed septa). Cyanosis is usually absent, *except as a terminal or transient phenomenon*, in patent foramen ovale and other localized defects in the interauricular and interventricular and aortic septa, and in patent ductus arteriosus, in all of which there is, in uncomplicated cases, a left to right shunt of arterial blood into the pulmonary circulation through the defect. Cyanosis is usually *entirely absent* in coarctation and hypoplasia of the aorta, anomalies of the aortic arch, subaortic stenosis, left-sided valvular lesions, and other anomalous conditions in which no abnormal communication between the two circulations exists, but in which the defect becomes of clinical significance by introducing pathological factors leading to cardiac or arterial strain.

Dyspnœa, though always present when cyanosis is advanced, does not appear to bear a definite relation to the degree of deficient aëration but evidently depends on some other factor as well. It is thus characteristic of many cases, such as patent ductus, patent foramen ovale, or septal defects, in which no trace of cyanosis is seen, shortness of breath and palpitation on exertion from early childhood, being quite frequently complained of. The same is true of *dyspnœic suffocative attacks* with

transient cyanosis which form an important diagnostic feature of cases of patent ductus.

Physical Signs.—The distinctive character of the murmur and thrill which may occur in many of those defects which are of clinical significance has been discussed under the individual lesions but may be briefly summarized. A *harsh, systolic murmur* and thrill localized over the upper part of the precordium and of diminished intensity or inaudible at the apex is characteristic both of pulmonary stenosis and of septal defects. It may in a few cases be heard best at the apex, and it may vary in rhythm, particularly in septal defects. Both in pulmonary stenosis and in patency of the duct the murmur usually has its maximum intensity high up over the second left interspace and may be heard beneath the left clavicle. That of auricular and ventricular septal defects is best heard over the third and fourth left interspaces. Murmurs of congenital lesions, when heard in the back, are usually due to patency of the duct or to septal defects. A *precordial thrill* with the same localization as the murmur is present in about 15 per cent. of congenital defects with physical signs, its presence as a rule corresponding to the degree of harshness of the accompanying murmurs.

In *defects of the interauricular septum* the murmur is often late diastolic or presystolic, and in patent foramen ovale presystolic and systolic murmurs may combine or alternate with each other, and may vary with change of position, their inconstancy supplying a differential point.

In *localized defects of the interventricular septum* a constant long harsh systolic murmur which does not vary in rhythm or quality, or with the position of the patient, and which has its maximum intensity at the third and fourth interspaces to the left of the sternum and audible in the left back but not transmitted to the axilla or into the vessels of the neck, and accompanied, in about one-third of the cases, by a rough systolic thrill, is characteristic. When such a murmur, so localized, is observed in a healthy young adult who presents no evidence of cardiac hypertrophy or other evidence of circulatory strain, it may be considered pathognomonic of "*Maladie de Roger*."

When *pulmonary stenosis and dextroposition of the aorta are associated with a defect of the interventricular septum* (tetralogy of Fallot), the murmur generated at the defect is transmitted along the aorta, and may usually be heard over the carotids in the neck.

In *patent ductus*, a harsh rumbling machinery murmur, beginning toward the close of systole and continuous throughout the cardiac cycle is present in a fair proportion of cases, and when it occurs is pathognomonic; in others the murmur is systolic or (rarely) diastolic. The pulmonary second sound is here usually accentuated and this helps to differentiate patent ductus from pulmonary stenosis, in which the pulmonary second is usually (not always) weak or absent. An abnormal area of dullness, in the first and second left interspaces (Gerhardt's sign), is also significant of the later stages of patent ductus, as indicating a dilated pulmonary artery. This sign may be produced also by retraction of an atelectatic left lung (Hochhaus), so is not positive unless confirmed by the roentgen-rays.

A powerful *diastolic* murmur and thrill with maximum intensity over the second and third interspaces, and an accentuated second pulmonary sound characterized several of the cases of abnormal communication between the lower part of the aorta and base of the right ventricle (*defect of the aortic septum*), and were probably the result of the pulmonary insufficiency that, in these cases, undoubtedly coexisted with the arterial-venous communication through the defect.

A *very harsh systolic murmur and thrill*, with maximum intensity at the *second right interspace* and transmitted into the vessels of the neck, persistent since early life in patients without rheumatic history and who do not present any generalized signs of obstruction at the aortic orifice, is significant of a *subaortic stenosis*.

Complete *transposition* of the arterial trunks has been diagnosed by the absence of physical signs in the presence of marked cyanosis, and an accentuated pulmonary second sound (Hochsinger).

Coarctation of the aorta is to be recognized by the evidences of the collateral circulation when this has been established, hypertrophy of the left heart, the frequent association of an acquired aortic insufficiency, a reduction in the force of pulsations and the blood-pressure in the legs as compared with the arms, a difference in height and volume between the radial pulses, the propagation of a prolonged systolic or postsystolic murmur and thrill along the dilated collaterals, and the presence of a systolic murmur (apparently generated at the site of coarctation), along the left sternal border, or with maximum intensity in the back, are other points diagnostic of coarctation.

The above are some of the indications by which type cases of the less complicated defects may sometimes be distinguished from each other. It must be remembered, however, that cardiac anomalies are frequently multiple, and that even in the uncomplicated cases, the features elicited by physical examination such as those referred to above, usually require confirmatory evidence before a positive differential diagnosis can be reached. For this reason we look with interest to the introduction of the newer methods of precision in this difficult field. Several positive findings have been recognized.

Graphic Methods.—*Roentgen-ray Examination and Orthodiagraphic Tracings.*—Definite information upon the existence of hypertrophy and dilatation of the various heart-chambers, dilatation of the pulmonary artery and its branches, dilatation of the ascending aorta, "high position" of the aortic arch and dextroposition of this vessel, and hypoplasia of the pulmonary artery or of the aorta is to be obtained from the skiagraph, which should be studied, for the correct interpretation of obscure cases, in both oblique positions and in 7-foot plates.

In the presence of dilatation of one or other of the two great trunks, the shadow above the heart shows a distinct widening to right or left of the median line. When the pulmonary artery is the one dilated, it appears under the roentgen-rays as a distinct bulging on the left side (second left arc) just above the curve of the left auricle, forming the so-called "roentgen-ray cap" of Zinn, which occupies the area of "Gerhardt's dulness" in the first and second left interspace. In well-marked cases of pulmonary

dilatation, the main pulmonary branches which enter into the formation of hilum of the lung are also widened and show in the roentgen-ray as broadened pulsating shadows (Assman's¹ sign). Such an enlarged and pulsating pulmonary arc is characteristic of most cases of patent ductus reaching adult life, but is not usually seen in patent ductus in infants, for the reason that the dilatation of the pulmonary artery is of gradual development and at this early age has not yet occurred. It is constant also in large defects of the interauricular septum and in this condition the aortic shadow is usually distinctly narrowed owing to the hypoplasia of the aorta that is practically invariably associated. An enlarged second left arc has also been described by the French authorities (Vaquez and Bordet, Laubry and Pezzi), as being characteristic of pulmonary stenosis, but the appearance is probably produced, in the great majority of cases, by the hypertrophied conus of the right ventricle (Usumotu), for most cases of pulmonary stenosis are of developmental origin and such usually present a hypoplasia and not a dilatation of the pulmonary tract. In the relatively small group of inflammatory pulmonary stenosis in which the narrowing is limited to the valvular orifice, the pulmonary artery is commonly dilated, and a prominent pulmonary arc is then the rule; but such cases form a very small percentage.

An enlarged first left arc (indicating a dilated left auricle) is a diagnostic *feature* of uncomplicated mitral stenosis; and *absence* of any prominence in this situation with great increase in size of the right chambers when combined with the signs of mitral stenosis suggests the presence of an "interauricular insufficiency" or complicating widely patent foramen ovale, and the radiograph is of the peculiar shape described as a magnified "*cœur en sabot*." Both this picture and that of the smaller "*cœur en sabot*" are characteristic of advanced cases of pulmonary stenosis with dextroposition of aorta and associated ventricular septal defect discussed above, in connection with the special symptomatology of these defects.

The shadow at the base of the heart shows a distinct widening in the presence of dilatation of one or other of the great trunks. When the pulmonary artery is the one dilated the widening appears as a distinct bulging on the left side "roentgen-ray cap" in the position of "Gerhardt's dulness." Dilatation of the aorta is indicated by an increased shadow to the right of the median line in the same situation. Conversely, hypoplasia of the pulmonary artery is indicated by a narrowing of the shadow to the left of the heart's base. These points and the typical shape which the ventricular portion of the heart assumes in the various valvular lesions are well shown in the heart-silhouette obtained by the orthodiagraphic tracing. Groedel² figured the outline obtained both in the various acquired valvular lesions and also in congenital pulmonary stenosis, patent ductus arteriosus, and coarctation of the aorta and points out that in ventricular septal defects there is no change observed at the site of the great vessels so that unless hypertrophy of the ventricles has occurred the silhouette is normal.

Fluoroscopic Findings.—Deneke³ diagnosed a case of interventricular septal defect in transposition of the arterial trunks by the appearance

¹ *Klinische Röntgendiagnostik*, Leipzig Vogl., 1922, pp. 74–98.

² *Deutsches Arch. f. klin. Med.*, 1911, vol. 103.

³ *Ibid.*, 1906, 39, 38.

on fluoroscopic examination. The heart showed a moderate degree of hypertrophy of the right ventricle, and this chamber formed the right border of the heart in place of the right auricle as normally occurs, so that the strong pumping movement of the ventricle could be seen on the *right* border as well as on the left, instead of the fluttering auricular movement normally seen in this situation. Deneke describes the appearances as follows: "In normal hearts the movement of the right border is seen on the fluoroscope as a sharp auricular twitching preceding the contraction of the left. Its character can be readily distinguished as auricular, *i. e.*, a short fluttering contraction followed by long, passive dilatation. The movement on the left border is slow, lasting much longer than that of the auricular, and is a strong pumping motion followed by a short delay in the contracted state, then a gradual dilatation which is slower than the ventricular contraction, but much quicker than the dilatation of the auricles." This phenomenon is not constant, nor, as Dietlen¹ has remarked, is it pathognomonic of ventricular septal defects, for it is seen also in certain other conditions of hypertrophy of the right ventricle. Nevertheless when this pumping action is present and pronounced, it directs attention to the possibility of a ventricular septal defect, *i. e.*, it yields confirmatory evidence, in the presence of distinctive physical signs.

The Electrocardiographic Curve in Congenital Hearts.—The following positive points may be said to have been elicited, and are sufficient to indicate the value of the cardiogram in this connection. (1) A "*negative initial Schwankung*" representing a reversal of the ventricular complex in that there is a *low R* and a deep exaggeration of the *downward S-wave* in Lead I, has been observed in many of the cases of congenital cyanosis, and was described by Nicolai and Steriopulo as pathognomonic of cardiac defects. It is merely significant, however, of the extreme right-sided hypertrophy which is invariably present in pulmonary stenosis and atresia, and present in practically all the more complex cardiac anomalies in which there is a free admixture of venous, blood with the arterial stream. A moderate degree of right-sided preponderance is characteristic of acquired mitral stenosis, but one does not meet there the extreme degree of hypertrophy of the right chambers met with in pulmonary stenosis, and the change in the electrocardiogram is correspondingly less. (2) *An extreme amplitude of curves in several leads* was observed by Lewis in congenital cyanosis and is described by him as a valuable sign of congenital valvular or septal defects. (3) The electrocardiogram in true (mirror-picture) dextrocardia when the heart is transposed upon itself, supplies the most positive sign of this abnormality that we possess. In this case Lead I is completely reversed upon itself, and Lead II takes the place of Lead III, exactly the same tracing being obtained as when the leads themselves are reversed in a normal individual. The transposed electrocardiogram decides clearly between this condition and a simple dextroversio cordis. For a comparison of the electrocardiograms in these two conditions see Fig. 51. (4) A high *P-wave* in Lead II, and

¹ *Herz. und Gefassen in Rontgenbild*, Leipzig, 1923.

usually slightly raised above the normal in Lead I, is significant of auricular hypertrophy and dilatation, and this has been found by P. D. White and others to be constant in pulmonary stenosis, in which the right auricle is always exaggerated. It is therefore a diagnostic sign of some value in this condition, and still more so we would suggest, in large defects of the interauricular septum, in which a dilated right auricle is a practically invariable feature while the changes in the right ventricle may be much less in evidence. (5) Left ventricular preponderance is significant of the hypertrophy of the left ventricle which occurs in left-sided valvular lesions and in many cases of coarctation of the aorta, and it therefore supplies a valuable differential point in the presence of obscure physical signs. (6) Partial or complete heart-block and minor abnormalities of rhythm have been reported in cardiac anomalies by a number of observers, and are undoubtedly due to the irregular disposition of the malposed fibres descending from the *a-v* bundle. The subject has been studied in ventricular septal defects by Morison, and in complete absence of the ventricular septum (*cor triloculare*) by Wilson and Grant. Minor irregularities in rhythm have been observed in persistent truncus by Mütze, and in ventricular septal defect with dextroposition of the aorta by Baumgartner.

In mitral insufficiency with patent foramen ovale, the *polygraphic tracing* may reveal a positive venous pulse in the neck. In the absence of auricular fibrillation or other signs of tricuspid insufficiency this is of value for diagnosis (Ohm).

Gas-analytic Methods.—An important diagnostic point between those defects due to abnormal communications between the right and left sides of the heart, and those due to pulmonary obstruction has been supplied by Plesch¹ working in Kraus' laboratory. In uncomplicated septal defects and patent ductus, there is usually an admixture of arterial blood with the venous current entering the lungs through the pulmonary artery, owing to the fact that under normal conditions the pressure in the aorta and left chambers is greater, so that blood passes from left to right through the defect. Plesch estimated the amount of oxygen in the alveolar air expired from the lungs, and found that in these conditions the venous blood passing to the lungs is reduced; that is to say, in terms of percentage of its oxygen content, the latter (O_2) is raised. On the other hand the alveolar air in cases of acquired valvular diseases and in one of congenital pulmonary stenosis showed no deviation from the normal. A method of ascertaining the blood-volume in the pulmonary circulation is urgently needed, for this would give positive diagnostic information as to the direction of the current in a case of suspected left to right shunt in compensated septal defects but no satisfactory method of ascertaining the gaseous content of the mixed venous blood has been obtained. The calculation of the amount of the venous arterial shunt, in cases of congenital cyanosis, has been discussed above under the special section on that subject.

The differential diagnosis between the cyanosis and clubbing of congenital cardiac disease and that of polycythemia vera, Ayerza's disease, pulmonary emphysema, cyanosis of enterogenous origin and other forms, is discussed under the section entitled "Cyanosis."

¹ *Berlin. klin. Wchnschr.*, 1909, **46**, 392.

Prognosis.—The duration of life has been considered in detail in connection with those defects that are of clinical interest, but a few generalizations may be made. The prognosis varies with the lesion and includes a wide range of possibilities, but is in general grave; this is based upon the direct interference with the circulation by the defect itself, and upon the well-known tendency of certain anomalies to become the seat of malignant endocarditis.

Among the least harmful forms of congenital cardiac disease may be mentioned anomalous septa in the auricles, hypoplasia and coarctation of the aorta with extensive collateral circulation, which may exist until past middle life without symptoms, frequently terminating then with a general failure of compensation under some undue strain. Localized uncomplicated defects of the interauricular, interventricular and aortic septa, and patent ductus arteriosus, in which conditions arterial blood passes into the pulmonary circulation from right to left through the defect, belong likewise to the more innocent lesions which may give rise to symptoms, or may be present indefinitely without producing any effect upon the circulation, becoming serious only upon the advent of some pulmonary complication raising the pressure in the right heart (producing a "*cyanose tardive*" or late *cyanosis*), or through the engrafting of a malignant endocarditis along the edges of the defects.

In the more complicated defects of the cyanotic group, in which a free admixture of venous blood with the arterial stream is a permanent state, and in which the prolonged effects of raised oxygen-unsaturation, polycythemia, increased viscosity of the blood and stasis in the peripheral capillaries, combine to produce the extreme form of congenital cyanosis, life is correspondingly shorter. Young's patient with cor biatriatum triloculare and anomalous septum attained the age of thirty-nine years, and Holmes' twenty-four years. Hedinger's case of tricuspid atresia with transposition of the arterial trunks and widely patent foramen ovale lived to the age of fifty-four years, and Rudolf's case of cor biloculare with transposition to twenty-one years, but these are rare exceptions, in which the combined anomalies have so interacted as to permit a degree of oxygenation compatible with the carrying on of life up to this time, although the unsaturation of the blood is permanently beyond the threshold value at which cyanosis appears; but the subjects of the graver defects, especially biloculate heart, transposition of the arterial trunks, aortic, mitral and tricuspid atresia, usually die in infancy or very early childhood. This is true also of persistent truncus arteriosus, although a patient reaching twelve years is recorded by Crisp. In pulmonary stenosis early adult life is not uncommonly attained, but is rarely passed, though here in exceptional cases life may be prolonged, Vulpian recording pulmonary stenosis, *rechtslage* of the aorta, and defects of the septum in a man who died at the age of fifty-two years. The average duration of life in pulmonary stenosis with ventricular septum closed is twenty and three-fifth years, and in pulmonary stenosis with ventricular septal defect ten and four-fifth years in our series of 96 cases; and among 31 cases of pulmonary atresia, the average duration of life for the cases with closed septum was twelve weeks and of the cases with ventricular septal defects

three and two-fifth years, the presence of the defect in the latter condition acting as an ameliorating factor. Finally, it is to be remembered that of the more complicated anomalies many subjects perish in the early stages of embryonic development, as only those in whom compensatory conditions arise survive until birth.

The prognosis depends largely upon the effects of the lesion upon the circulation, that is, upon the amount of cardiac strain or the degree of oxygen-unsaturation induced by the defect, and upon the compensatory powers. For this reason symptoms will frequently prove a better guide to the immediate future than physical signs. Such conditions as septal defect may give marked murmurs and thrill, yet lead to no hampering of the heart's action and to little interference with oxygenation until some additional factor, such as obstruction in the pulmonary circulation supervenes producing a *transient* or *terminal* cyanosis. Persistent cyanosis, a continued low temperature, a marked increase in the number of red blood cells (above 5,500,000), and dilatation of the heart, all point to a grave disturbance of the circulation and to a rapidly fatal issue. On the other hand, the entire absence of cyanosis and its attendant phenomena does not always argue a favorable prognosis, for in such cases sudden death may occur without any warning, either quietly, or in a paroxysm of cyanosis with dyspnoea. The embarrassment to the circulation which the lesion itself entails is not the only source of danger. Grave danger lies also in the frequent intercurrent of a bacterial endocarditis in those patients who attain early adult life, and in the fact that infections or broncho-pneumonia are apt to prove rapidly fatal. The liability of patients with pulmonary stenosis to tuberculosis, and the frequent termination by sudden cerebral complications, are other unfavorable factors. These considerations indicate the extreme gravity of the more pronounced cases, and the fact that even in the more innocent forms of congenital cardiac disease the prognosis must be framed with reserve and caution. Among the better class, where good hygiene prevails and the most suitable conditions of living can be sought, the outlook is better than among the children of the very poor.

TREATMENT

The treatment of congenital cardiac disease is *preventive* rather than remedial and attention must be directed first to prenatal care, and next to the protection of the individual with a congenital lesion from influences which may tend to exaggerate it or increase the cardiac strain which it induces. Further it may attempt the *alleviation* of the distressing symptoms of increased oxygen-unsaturation under which the subjects of the so-called cyanotic group invariably labor. Lastly, the question of improvement or radical cure of certain grave defects by *surgical intervention*, must be considered.

Prenatal Care.—This involves not only the guarding of the prospective mother from infections and the shielding of her during the critical early weeks of pregnancy from all possible sources of these and from physical and emotional trauma. It implies also the actual prevention of concep-

tion between individuals who are themselves diseased, are the victims of alcoholism or other poisons, who are grossly illimated or related by ties of immediate consanguinity. Statistics show that cardiac anomalies are only rarely, ancestral qualities, but are usually the result of disease of the germ-plasm or of mechanical interference with intra-uterine growth, the result of pathological changes in the parental organism or in the environment of the embryo.

The evidences of gross myocardial disease in many of the graver cases of congenital stenosis and atresia, with Warthin's demonstration of the heart muscle as the favorite habitat of the spirochete in congenital lues, and the evidence of the frequency of rheumatic heart disease in pregnancy, indicate that cardiac defects of the inflammatory type are very commonly the result of disease in the parents and directly transmitted to the offspring. These factors should be kept clearly in mind in preventive therapy. Rigid serological investigation of both the pregnant mother in whom syphilis is suspected and of an infant in whom cardiac defects are detected, is indicated with a view to vigorous antiluetic treatment.

Preventive Treatment of the "Non-cyanotic" Group.—In the relatively large group in which cyanosis is absent the expectation of life is good so long as the patients keep within the limits of their reserve force, and so long as the vicinity of the defect does not become the seat of an endocarditis or endarteritis. They should therefore be given the same protective care and preventive treatment as is given to young patients with healed rheumatic lesions to guard against overstrain, while a strict watch is kept against focal infections, especially from teeth and tonsils. Colds and exposure to the usual diseases of childhood, especially infections such as measles which tend to involve the respiratory tract, should be avoided.

Treatment of Cases of the Cyanotic Type (Morbus Cœruleus).—This must be symptomatic or palliative or preventive in the sense that the inevitably downward course may be retarded by the maintenance of the best possible hygiene and the avoidance of complications. All the precautionary care noted above is indicated, remembering that, in the majority of cases cyanosis develops after some accident which increases the pulmonary obstruction or lowers the systemic pressure (thus favoring the venous-arterial shunt).

A carefully regulated life, a plentiful supply of light, fresh air, and warmth, the maintenance of an equable bodily temperature, the avoidance of mental agitation and of undue physical exertion, rest and quiet forms of exercise, where this last is permitted by the condition of the patient, are all essential. The diet should be carefully ordered, light and nutritious. Free action of the excretory organs, especially of the skin, should be promoted and the child kept clothed with flannel. Sudden changes in the external temperature must be avoided and, when possible, resort should be had to a warm winter climate. When adult life is attained choice of light employment which does not call for sudden or great physical exertion is important. In women child-bearing is fraught with danger. The mother of the cyanotic child should be taught that *character-building* is essential to the prolongation of its life and trained accordingly. The child should be taught to keep his exertion below the tolerance limit.

Of symptomatic measures for the relief of the cyanotic group, venesection may be required to relieve the overloaded right heart; and the application of leeches over the liver often gives great relief. Various remedies may be of use; for dyspnoëic attacks diffusible stimulants should always be kept at hand, and in infants the hot mustard bath is helpful; epinephrine may be given in the frequent attacks of syncope. Sedatives may be necessary for the troublesome cough and nervous irritability and hypnotics for the insomnia which is sometimes marked in older subjects. *Inhalation of oxygen* is of no direct benefit in congenital cyanosis, in which oxygen-unsaturation is due to a stream of venous blood entering the arterial stream after this has left the lungs; nevertheless it should always be tried, in the first place because there may be a pulmonary factor, such as an associated atelectasis; and secondly, the lack of adequate response to oxygen-intake by the respiratory tract in these cases of venous-arterial shunt, makes it a valuable test for diagnostic purposes.

Direct intravascular administration of oxygen has been carried out successfully in experimental animals both by the intra-arterial (C. A. Lumsden) and by the intravenous route (Galata) but it has not been attempted, so far as we know, in the human subject. Could this be rendered safe and practical it would secure the same alleviation that is derived from oxygen inhalation in cyanosis of pulmonary origin.

Surgical Treatment.—The great advances made in the past twenty years, both in the differential diagnosis of cardiac anomalies, and in the domain of cardiac surgery, open up possibilities for the improvement or even the radical cure of some of the graver conditions. We refer especially to the experimental work by Carrel and Tuffier¹ by which the pulmonary orifice could be enlarged by patching the wall from without (with aorta or vena cava from another source) and incising the stenosed valve, and to the success of Cutler and Levine² in relieving the symptoms of mitral stenosis by entering the left chamber by the "blind intraventricular route" (near the apex and avoiding the left papillary muscle), and incising the mitral orifice. Surgery may be possible in pulmonary stenosis of the valvular type, in which the orifice lies so close to the chest wall, but here the differential diagnosis is important from the commoner developmental forms, in which hypoplasia of the pulmonary tract and conus stenosis present complicated conditions that yield little hope for operative interference.

Operative interference in patent ductus arteriosus in the form of ligation of the duct, was suggested by Munro on the ground that a probable diagnosis is now possible and that the vessel lies in an accessible situation. The fact that distinctive signs occur only after pulmonary dilatation has taken place and a certain adjustment of the vessels to the new order of the circulation has set in, would make one hesitate to resort to so radical a measure. Resection of the obliterated ligamentum arteriosum in cases of right aortic arch with symptoms of obstruction of the œsophagus has been suggested and could readily be carried out if the diagnosis is made; Arkin has demonstrated that this is feasible.

¹ *Jour. Exper. Med.*, 1914, 20, 3; *Ibid.*, 1921, 34, 441.

² *Arch. of Surg.*, 1924, 9, 689 (with full bibliography and historical and experimental data).

CHAPTER XXII

DISEASES OF THE ARTERIES

BY THE LATE SIR WILLIAM OSLER, BART., M.D., F.R.S.

REVISED BY

CAMPBELL P. HOWARD, M.D., C.M.

ACUTE ARTERITIS

MISTAKING staining of the intima for inflammation, the older writers described arteritis as a common event in many diseases. In the early years of the nineteenth century Cruveilhier and others believed that it was the cause of the clotting of the blood in the vessels, and that it arose spontaneously as a complication in the fevers. Virchow took an opposite view, viz., that the thrombosis was the primary event, and the arteritis always secondary, whether the clot was embolic in origin or formed at the site from conditions of the circulation or the blood. Of late years we have recognized that the arteritis is sometimes a sequel of the clotting, sometimes due to primary changes in the vessel wall.

Secondary Arteritis.—Secondary arteritis occurs when a local infection attacks the vessel wall from without, as in abscess formation, in the pulmonary vessels of lobar pneumonia or acute miliary tuberculosis, and in the cerebral arteries of septic, tuberculous or other forms of meningitis (McMeans¹), when periarteritis and subsequently endarteritis result; or when the intima is injured and inflamed as a result of an infected embolus or an infected marantic thrombus. This form will be considered in connection with embolism and thrombosis, in the course of which it is an incident.

Primary Arteritis.—Primary arteritis is a rare disease, met with as a complication in the acute infections, and occasionally as an independent malady. In ordinary medical work it is most frequently seen in typhoid fever, but its rarity may be judged of from the fact that in this disease there were only 5 instances in 1500 cases at the Johns Hopkins Hospital.² In smallpox, scarlet fever, influenza, and pneumonia, cases have been observed. It is less common in rheumatic fever, chorea, diphtheria, yellow fever, typhus, gonorrhœal septicemia, and measles. In typhoid fever, pneumonia, and diphtheria the organisms of the disease have been found in the vessel wall. In direct infection from the blood the intima is first involved, and there may be small vegetative out-growths such as we see on the intima of the valves, but this is rare. In other cases the infection is conveyed through the vasa vasorum, and the adventitia and media are first involved. The grades of alteration in the vessel depend upon the type and virulence of the organism. The intima alone may be affected

¹ *Am. Jour. Med. Sci.*, 1916, **151**, 249.

² W. S. Thayer, *Johns Hopkins Hosp. Bull.*, 1904, **15**, 323.

with the result of the formation of a thrombus; in other cases the vessel wall is acutely inflamed and there are swelling and infiltration of the neighboring tissues.

Symptoms.—The symptoms depend upon the vessels affected. In the external arteries, as in the femorals or popliteals, for which there is a predilection in typhoid fever, there is pain, often of great severity in the course of the vessel, spontaneous or on movement, and an increase in the fever with swelling over the vessel and sometimes redness. The pulse below is obliterated; the limb is at first pale and cold, and then gradually becomes livid at the periphery. When the femoral is obliterated, whether or not gangrene follows will depend upon the rapidity with which the vessel is blocked, and the extent of the thrombus. There are cases which look threatening at first, and in a few days the signs of obstruction pass away. In other instances the process extends and both legs may become affected. In rheumatic fever, according to Barie,¹ the carotids and the vessels of the arm are more frequently attacked, and manifested by fever, pain on palpation, throbbing and perhaps a thrill, with some dilatation.

Gangrene is only too apt to follow obstruction of the femoral artery in the acute infections. It is not always easy to determine whether the thrombosis results from a primary arteritis or an embolus. Suddenness of onset and the existence of conditions favorable to embolism point to the latter. There are cases in which the onset is severe, and for a few days the symptoms suggest that gangrene will follow, and then the circulation is reëstablished and color returns to the limb. Parietal thrombosis with only partial occlusion of the vessel may be present. Of our 2 cases of typhoid fever in which the femorals were affected, gangrene followed in one, in the other the condition cleared in a few days. In 1 case the brachial was involved at the bend of the elbow.

Arteritis of the internal vessels is still more rare. Of 2 of our cases in which the cerebral vessels were affected in typhoid fever, in 1 on the ninth day of the disease, in the other on the nineteenth, both proved fatal. In the arteries of the kidney, the spleen, and occasionally of the heart, a spontaneous clotting may occur as a result of inflammation in the acute infections.

Primary Multiple Arteritis.—There are instances in which in the course of a few days, without the existence of any local disease, a thrombo-arteritis occurs in many vessels, associated with high fever and signs of an acute infection. The senior writer² reported a remarkable case in a man, aged twenty years, who had had typhoid fever two years previously. He was admitted with fever, rapid pulse, diarrhœa, and abdominal pain. He had thrombosis of both femorals and iliac arteries and of the lower 2 inches of the abdominal aorta, and of two large branches of the splenic artery. There were infarcts in the spleen and in the kidney.

Acute Aortitis.—Lesions of the aorta due to acute inflammation are exceedingly rare. The term aortitis has been used very loosely to describe conditions which are degenerative rather than inflammatory, and which come under the general category of arteriosclerosis. It is an altogether false conception of the process to speak of the degenerative plaques of

¹ *Paris Médical*, 1913, 11, 114.

² *Tr. Assn. Am. Phys.*, 1887, 2, 133.

the intima and the foci of medial necrosis met with so commonly in the infections (typhoid fever and influenza for example) as acute aortitis. The process occurs under the following conditions:

1. **Acute Vegetative Aortitis.**—In pneumonia, in rheumatic fever, and in the acute septic infections, the lining membrane of the arch may present numerous irregular vegetations identical with those on the valves. The condition is rarely if ever met with apart from aortic or mitral valvulitis. It is exceedingly rare, and the senior writer did not see more than three or four instances. The outgrowths may be firm and warty in character, or a perfectly smooth intima may present a series of globose vegetations. Acute aneurism may be associated with the process. There may be half a dozen small sacs. Cases have been reported, particularly in France (Minet et Pellissier¹) and America (Klotz²), in connection with rheumatic fever. Pneumococci and staphylococci have been found in the vegetations.

2. **Acute Mesaortitis.**—This is much more common, particularly in syphilis. Within a few weeks a localized productive aortitis occurs, largely confined to the media, but quickly involving the other coats, and leading to aneurism or to an acute dilatation of the part of the vessel affected, or to rupture with a dissecting aneurism. This is a type of aortic disease to which the term "acute aortitis" may very properly be applied, and will be dealt with under the subject of aneurism. Other varieties of acute infective mesaortitis are conveyed through the vasa vasorum and there are foci of softening, sometimes of acute suppuration, in the middle and outer walls of the artery. This may lead to localized weakening, so that the intima over the spot is split. As many as four, five, or six of these small fissures may be seen on the intima of the arch, each one leading into a little focus of softening and dilatation. Sometimes the edges of the splits are covered with luxuriant vegetations. Acute aneurism is apt to follow, which may rapidly prove fatal. To this condition, occurring in the course of an infection like rheumatic fever, the term "acute aortitis" is really applicable. There are instances in which in an aorta with perfectly smooth intima there is a small erosion like an acute ulcer, leading directly into an aneurism. The senior writer³ reported a remarkable case, in which in the lower part of a normal looking descending aorta there was a linear perforation 1.5 cm. in extent, which led directly into a small aneurismal sac which had ruptured into the œsophagus. The woman was only thirty-five. There was no endocarditis. The probability is that she had an acute mesaortitis comparable with that which may be produced in animals experimentally, and that over this small spot the intima fractured.

Symptoms.—The symptoms of acute aortitis may be vague. It is interesting to read the extended description of the disease as given by French writers, and then to note the silence of American, English, and German authors on the subject. In syphilis, the pain, often anginal in character, and the development, under observation, of aortic insufficiency, give decided indications of disease at the root of the aorta. In rheumatic

¹ *Rev. de Mèd.*, 1920, **37**, 287.

² *Jour. Path. and Bact.*, 1913, **18**, 259.

³ *Lancet*, 1910, i, 840.

fever or acute sepsis, signs indicating acute dilatation of the arch of the aorta are suggestive. A large majority of cases of so-called aneurism occurring in children in connection with rheumatic fever, are instances of dynamic dilatation of the aortic arch in connection with aortic insufficiency. Sansom¹ considers that the pain of acute aortitis differs from angina pectoris of atheromatous origin in that it is provoked or aggravated by very slight exertion, and may be unassociated with high arterial tension; he also calls attention to the peculiar dead-leaf hue of the countenance and to the more marked facies Hippocratica. Attacks of dyspnoea with a sense of oppression in the chest are usual. Retrosternal dullness may develop rapidly. Paroxysmal dyspnoea is present only when syphilitic aortitis is associated with aortic insufficiency or aneurism of the root or arch of the aorta, according to Keefer and Resnik.² Neuman³ reported 29 cases of non-syphilitic aortitis in patients under forty years of age in whom the following symptoms were considered diagnostic: retro-sternal pain, dyspnoea, cough, tachycardia and irregular fever, seldom reaching above 101° F. The more important physical signs are suprasternal pulsation, a widening of the aorta both on percussion and in the roentgenogram; a soft-blowing or a rough systolic murmur over the aortic cartilage which is intensified or rendered audible with the patient in the upright position with the hands on the head (Kukovieroff); a bell-like accentuation of the aortic second sound, and tenderness over the sternum. Pressure symptoms may appear late in the course of the disease.

An abdominal aortitis is recognized by French writers, characterized by pain, throbbing, increased mobility, and a loud systolic murmur, with a relatively higher blood-pressure in the femorals than normal. Clinically, the condition is quite as vague as the acute thoracic aortitis.

A special form, *tuberculous aortitis*, may be mentioned, of which some 20 cases have been described (Flexner;⁴ Blumer;⁵ Woolley;⁶ In Flexner's case there was a small tuberculous nodule just below the left subclavian artery, seated directly on the intima, which everywhere else was smooth. Tubercle bacilli and giant cells were present and there were tubercles in other organs.

3. **Acute Periaortitis.**—Occasionally in suppuration in the neighborhood of the aorta, as in connection with a lymph gland in the anterior mediastinum or in suppurative processes in the abdomen, the adventitia of the aorta may be involved, and present a focus of suppurative softening.

Treatment.—In the very acute cases there is no help: in the subacute and chronic types morphine and antipyrine may be used in appropriate dosage. Sansom recommends the prolonged administration of either sodium or potassium iodide (gr. v to x, 0.3 to 0.6 gm.). Meyer⁷ and others have found sodium citrate (3 to 4 gm.), administered by mouth or intravenously, of some assistance in both arteritis and vascular spasm.

¹ *Lancet*, 1899, ii, 1075.

² *Arch. Int. Med.*, 1926, **37**, 264.

³ *Jour. Am. Med. Assn.*, 1925, **85**, 1361.

⁴ *Bull. Johns Hopkins Hosp.*, 1891, **2**, 120.

⁵ *Am. Jour. Med. Sci.*, 1899, **117**, 19.

⁶ *Bull. Johns Hopkins Hosp.*, 1911, **22**, 82.

⁷ *Ann. Surg.*, 1916, **63**, 280.

CHRONIC ARTERITIS. ARTERIOSCLEROSIS

Definition.—A general disease of the arteries, characterized in the small vessels by thickening of all the coats, and in the larger by gelatinous swelling, necrosis, fatty degeneration and calcification, the processes to which the name *atheroma* has been given.

Sometimes the term arteriosclerosis is limited to the smaller vessels, and that of atheroma to the larger arteries. On account of the irregularities due to calcification and atheromatous erosions, the name of *endarteritis deformans* (Virchow) is given to the process in the larger arteries.

Etiology.—There are four great factors in the causation of arteriosclerosis—the normal wear and tear of life, the acute infections, the intoxications, and those combinations of circumstances which keep the blood tension high.

1. **Wear and Tear of Life.**—Among organs the bloodvessels alone enjoy no rest. Not only does a ceaseless rush of fluid pass through them at a speed of 10 inches a second, but the walls of the main pipe are subjected to a distending force of 25 pounds to the square inch, 60 to 80 times a minute, 80,000 to 100,000 times in the twenty-four hours. The heart has rest in diastole, but distended by the charge from the left ventricle, the arteries pass it on partly by the natural elasticity of the walls, partly by an active contraction of the muscle fibres. Like other organs they live under three great laws—use maintains and in a measure sustains structure; overuse leads to degeneration; in time they grow old, in threescore or in fourscore years the limit of their endurance is reached and they wear out.

The stability of tubing of any sort depends on the structure and on the sort of material used; and so it is with the human tubing. With a poor variety of elastic and muscular fibres in the bloodvessels, some are unable to resist the wear and tear of everyday life, and have at forty years of age arteries as old as those of others at sixty. One day, at a meeting of the American Medical Association, Dr. Henry Martin (of vaccine fame), who possessed all histrionic gifts, was demonstrating samples of Esmarch's bandages, one of which, as he spoke, he broke into fragments with great ease, while another resisted all his efforts. "They look the same," he said, "and they are made of the same substance, but they are not the same, one is shoddy, the other is the genuine article." And so it is with our arteries. They look the same macroscopically and microscopically, but they differ in different individuals in the quality of the materials used and the capacity to resist the ordinary stress of life. Not only are there individuals, but whole families, with "shoddy" bloodvessels. Hence the truth of the old saying attributed to Cazalis, "a man is as old as his arteries." In the building of the human body, as of chaises, there is, as the Autocrat says, "always somewhere a weakest spot," and too frequently this is in the circulatory system.

The conditions of modern life favor arteriosclerosis, as a man is apt to work his body machine at high pressure, and often takes less care of it than of his motor. The best express engine from the Baldwin works run day by day at maximum speed will not last one-tenth of the time

it would do if it were not so pushed. But nowadays, with the human engine it is top-speed or nothing, and we cannot wonder that it early shows signs of hard usage. In the fourth or fifth decade, even with the best of habits in eating and drinking, the incessant strain and anxiety of public life or of business may lead to degeneration of the bloodvessels. The recent statistical proof that the average age of death in American men has diminished testifies to this. Mental exertion is not of itself injurious, and the life of the student need not be one of great tension, but the mental exertion of the modern business man is of a different kind. Competition is so keen and the environment so stimulating that, even without social or political ambitions, high pressure seems a necessity. The tragedies of life are largely arterial. Represented in the old mythology as winged, Nemesis, the goddess of the Inevitable, may still be pictured with a wheel, the wheel of life, to the ceaseless revolutions of which the circulation ministers. How often does her fatal touch call away in their prime the best and the bravest—men whose only fault has been the unselfish abuse of the body machine!

After forty it is exceptional to examine the arteries without finding evidence of degeneration—here and there a small plaque of atheroma, an occasional streak of intimal fatty degeneration, and with this the mitral and aortic cusps may have lost just a little of their delicate tenuity. With advancing age the arteries become thicker and the atheromatous changes more marked. As a rule, in the very aged not only the smaller arteries are thickened, but the aorta and its main branches show extensive changes with calcification. Occasionally, however, a very old person may have singularly healthy bloodvessels. It is not the case, as so often quoted, that Harvey found the vessels of Parr, who lived to be one hundred and fifty-two (?), to be healthy. He does not mention them. Living quieter lives and with less stress and strain, women are not so frequently the subjects of arterial changes, and in consequence they last longer. In infants and young children arteriosclerosis occurs: (1) As occasional patches or flakes, or even calcified foci, in the vessels of the new-born. (2) In infants dying of the acute infections, streaks of fatty degeneration of the intima and foci of necrosis of the media are not uncommon. (3) Widespread arteriosclerosis of the smaller vessels may occur without nephritis and without recognizable cause. Two or three cases may occur in the same family. (4) In congenital syphilis, diffuse or localized sclerosis of the arteries may occur, sometimes early, sometimes as a late manifestation. Fremont-Smith,¹ who reviewed the literature of arteriosclerosis in the young, found no difficulty in collecting 144 cases.

2. The Acute Infections.—Of the acute infections, *syphilis* is the one with a special predilection for the arteries. There are changes best described as acute productive arteritis, and there are degenerative changes which come in the category of chronic arteritis. The special features of syphilitic aortitis will be described later. The lesion may be a chronic obliterative endarteritis, limited to a special group of vessels, as in the brain, the heart, or the vessels of the extremities. Extensive

¹ *Am. Jour. Med. Sci.*, 1908, **135**, 199.

arteriosclerosis in infants and in children is very often syphilitic, and in the acquired disease a slow, progressive arteriosclerosis may exist in combination with other parasymphilitic manifestations. We have learned to recognize the great frequency in *scarlet fever*, *measles*, *diphtheria*, *small-pox*, and *influenza*, of foci of arterial degeneration. It has long been known that in *typhoid fever* areas of necrosis and fatty degeneration are met with in the aorta. The observations of Thayer show how important are the cardiovascular relations of this disease. Of 52 postmortems, evidence of sclerosis was present in 30, and in 21 of these the changes looked recent. It is remarkable that out of 62 instances in which the condition of the coronary arteries was stated, in 19 sclerotic changes were present, and in 13 of these the changes were recent. One of our house physicians died at the end of the third week of typhoid fever. There were patches of endarteritis at the root of the aorta and numerous patches of yellowish sclerosis in both coronary branches. Thayer examined 189 patients who had had typhoid fever in the hospital within fourteen years, and 40 per cent. of the persons between the ages of ten and fifty presented palpable radial arteries compared with 17.5 per cent. of a series of control cases. The change may be in connection with the higher blood-pressure which he found to prevail in these patients.

At the Franz-Joseph Hospital, Vienna, Wissal examined 300 bodies of children dead of acute infections, and in 80 found signs of arteriosclerosis, usually in the form of ordinary patches in the aorta and larger branches, but the small vessels were also found involved. He found the chief changes, which were in the media, to bear a striking resemblance to those produced in experimental aortitis in animals.

Tuberculosis is another disease with which arteriosclerosis is frequently associated. It has been observed by many writers that in chronic pulmonary tuberculosis the superficial bloodvessels are apt to be thickened. It is rare to examine a patient with tuberculosis of the lungs of more than two or three years' standing without finding thickening of the superficial arteries.

Experimental production of arteriosclerosis by the various bacterial toxins affords an explanation of this gradual production of sclerosis in the chronic infections. The importance of constant absorption of such products from a chronic suppurating sinus, septic teeth or gums, a chronic colitis and so forth, cannot be overstated.

3. **Intoxications.**—Of the poisons which have an important influence on the bloodvessels, some are exogenous, others endogenous. Of the special exogenous poisons, alcohol, lead, and tobacco, the first named is very generally regarded as a potent influence in causing degeneration of the bloodvessels. In man it is very difficult to separate effects of *alcohol* from those of other causes and there has been a strong revolt against the popular belief. It must be confessed that it is difficult in any given case to furnish evidence that alcohol alone is the cause. For example, in a middle-aged man who has drunk freely, eaten largely, and worked hard, it is impossible to say which of these factors is responsible for the degeneration of the bloodvessels.

Tobacco is another poison about which it is very difficult to get conclusive evidence. Experimentally, it is easy to produce the most extensive degeneration of the aorta in animals with nicotine. When one considers the extraordinary quantities consumed over long periods of years by men who show no trace of vascular change, or not more than the ordinary wear and tear of life would warrant, it is difficult to believe that tobacco can have a very important influence. It rapidly raises tension and may cause spasm of the arteries, which factor may account for the cases of sudden death in young or middle-aged men in whom excessive use of tobacco has been the only etiological factor. Angina pectoris is sometimes associated with abuse of tobacco, and the influence may be, as Huchard and others believe, through inducing an arteriosclerosis of the coronary arteries.

Lead has a very important effect upon the bloodvessels. A slow, gradual sclerosis is common among painters and others who take a small quantity of lead into their system. There are three elements here to be considered: the direct toxic action of lead on the bloodvessels, the disturbance of metabolism which leads to gout, and the chronic interstitial nephritis, all of which are associated with high tension and favor sclerosis. Of other exogenous poisons, tea and coffee are supposed to have an influence, but it is not easy to get conclusive evidence of the connection.

Of endogenous poisons that may promote arteriosclerosis may be mentioned all the conditions of perverted metabolism. The thickening of the arteries in *gout*, in *diabetes*, in *chronic nephritis*, in *obesity*, may be due to the action on the bloodvessels of poisons retained within the system. Loeper¹ has drawn attention to a number of substances, such as oxalic acid, lactic acid and extracts of putrefying flesh, all of which produce atheroma experimentally.

4. Conditions that Keep up High Blood Tension.—Within limits, the pressure with which the blood circulates in the arteries varies very greatly, in order that the circulation may adapt itself to the varying conditions of life. Healthy individuals differ in the degree of the blood-pressure, but one rarely finds it above 150 mm. Hg. The pressure varies, too, at different periods of life, and as age advances the blood-pressure rises. Sir Clifford Allbutt² discussed this feature in a most suggestive paper. There can be no question that in many individuals the rise in pressure antedates the appearance of the arteriosclerosis, as so frequently emphasized by Allbutt.³ In addition to this "essential hypertension" group, we recognize two others, in one of which the high tension is associated with consecutive cardiac and renal disease, and in the other it is secondary to some forms of chronic nephritis in association with cardiovascular disease.

The following are some of the causes of this hypertension; (1) *Over-eating*: Excess of food and drink acts in two ways, first by keeping the bloodvessels constantly distended, and secondly, in the processes of primary and secondary metabolism substances may be formed which are

¹ *Arch. des mal. du Cœur*, 1908, **1**, 45.

² *Medico-Chirurgical Soc. Trans.*, 1903, **86**, 323.

³ *Diseases of the Arteries* (McMillan & Co.), London, 1915, **1**, 154.

directly toxic. Attention has been repeatedly called to the frequency of arteriosclerosis in persons who have been temperate in every respect except at the table. It is well known to caterers that teetotallers eat much more than other people, and in the United States arteriosclerosis is very frequent among the well-to-do classes, who, as a rule, are abstemious so far as alcohol is concerned, but exceedingly careless and indulgent in the matter of eating. The writers' experience is fully in accord with that of Allbutt, that "one main cause of rising arterial pressure in middle life is excess of feeding, that is to say, of food in excess of work and excretion." The express engine capable of running fifty to sixty miles an hour if stoked for that purpose and put into the station yard to "shunt" empty cars will go to pieces very soon. This is what so many of us do with our engines. We supply the fuel for fifty miles an hour and run the engine at ten miles. In our bodies, as in the engine, damage is certain to follow from the accumulation of waste and the disproportion between intake, work done, and output. For the statement that meat eaters are more prone than others to arteriosclerosis we have no positive warrant, but the Indians and Japanese, who subsist chiefly on a vegetable diet, are said to be much less affected than Europeans.

(2) *Muscular Effort*.—In no way is blood-pressure more surely heightened than by the persistent use of the muscles, but we must be careful not to draw hasty conclusions. A majority of laboring men have a blood-pressure from 30 to 50 or 60 mm. of Hg. above that of rest during the greater part of the day. This is well within the normal limits, and cannot be hurtful. It has been determined by roentgen-ray observations that calcification of the arteries of the upper limb occurs more on the side most frequently used. It is the very severe muscular efforts repeated over-prolonged periods that damage the cardiovascular system, the conditions that produce the hypertrophy of the heart, as in miners, mountain climbers and athletes. The difficulty here is to separate the effect of muscular effort from associated conditions of overeating, alcohol, and tobacco. The possibility has to be considered of *overactivity of the adrenals*, in which an increase in the amount of the internal secretion, which keeps up vascular tone, causes hypertension and finally sclerosis. So far this is a purely hypothetical conception. The influence of vagus irritation upon the development of arteriosclerosis at the root of the aorta, at least in the laboratory animal, has been advanced by Shaw.¹

Etiologically, then, there are three great groups of arteriosclerosis as recognized by Allbutt: first, the *involutionary* (decrecent or senile), in which the degeneration is caused by the ordinary wear and tear of life, and which is as natural as gray hair and failing eyesight; secondly, the *toxic* group, in which the degenerations are caused directly by the poisons of acute and chronic infections and of the intoxications; thirdly, the *hyper-pietic* group, in which the degeneration follows persistent high arterial tension. Practically in a given case of arteriosclerosis, in a man of, say, fifty-five, two or all three of these factors may be present, and it is exceedingly difficult to assign to each their relative value.

¹ *Quart. Jour. Med.*, 1925-1926, **19**, 203.

Pathology.—It is rare to find the arteries entirely free from disease. Even in children small flecks of atheroma or fatty degeneration of the intima are by no means uncommon. In the bodies of middle-aged persons some arterial degeneration is always present, and, as a rule, the older the individual the more pronounced they are. In extreme old age calcification may be a widespread process, but occasionally the vessels of persons above eighty years of age show very little atheroma.

While arteriosclerosis is a general disease, affecting, as a rule, all of the arteries, the process may be much more advanced in some vessels than in others. The arteries of the brain may be stiff and hard, while those of the abdominal organs show no change; or the vessels of the limbs may be stiff and rigid, while the intima of the arch is smooth. The coronary arteries may be extensively diseased in comparatively young persons, while there are no changes in the other vessels. As a rule, this limitation of the disease to the vessels of one organ or to a limited portion of the large arteries is characteristic of syphilis; but there are instances in which this disease can be excluded with reasonable certainty.

In the *larger arteries*, the aorta for example, the following are the important changes: (a) Small areas of fatty degeneration of the intima, of a yellowish color, not raised. This may be the only lesion present. (b) Gelatinous-looking raised areas scattered over the intima, and seen particularly about the orifices of the arteries. They are translucent, and on section are seen to be confined to the intima. (c) Larger plaques of yellowish color due to fusion and fatty degeneration of b. (d) Calcified plaques. (e) Areas of atheromatous softening, which may project above the level of the intima, and which the old writers called atheromatous pustules. (f) Open atheromatous ulcers, usually flat and due to the breaking down of foci of atheromatous softening. In advanced cases the inner surface of the aorta is rough and irregular from the presence of calcified plates and areas of softening. In rare instances, as in a case reported by Bunting,¹ there is formation of true bone with even a cellular marrow as found normally in cancellous bone. (g) On section of the vessel the changes are found to be chiefly in the intima, but the media is usually atrophied, sometimes with foci of necrosis and areas of calcification, sometimes of true ossification. The adventitia is thickened and indurated, but necrosis and calcification are rarely seen in it. In many instances we find all grades and phases of the process going on side by side. The artery, may be dilated, and sometimes there are small aneurismal bulgings.

In the *smaller arteries*, particularly of the lower extremities, the Mönckeberg type of arteriosclerosis is frequent; in this type there is first degeneration of the muscular elements and then a deposition of fat and finally of lime salts which become fused into rings, replacing the media.

Experimental arteriosclerosis has thrown a great deal of light upon the mode of production of the disease.² Inoculation with cultures may produce proliferative changes in the media with thickenings of the intima.

¹ *Jour. Exp. Med.*, 1906, 8, 365.

² Klotz in his monograph on "Arteriosclerosis" (*Publications from the University of Pittsburgh*, 1911) gives a masterly review on experimental as well as human arteriosclerosis.

Diphtheria toxin, on the other hand, causes degenerative lesions affecting chiefly the media and adventitia followed by calcification. The most remarkable degenerative changes follow the use of epinephrine and other agents which raise the blood-pressure. Here the media is involved, necrosis of elastic and muscle fibres takes place, with fracture and splitting of the same with early calcification. Aneurisms are formed either by direct bulgings over areas of disease of the media or from splits of the intima.

Newburgh and Squier¹ found that rabbits which were fed on a high protein diet for a number of months, developed arteriosclerosis in the aorta which histologically resembles that of the human type; they did not regard the contained cholesterol as the sole cause.

Recent researches lead to the conclusion that in the ordinary type of arteriosclerosis the primary lesion is in the media, either productive or degenerative. To compensate, a reaction occurs in the intima with hyperplasia of the subendothelial connective tissue which undergoes hyaline, fatty, and calcareous changes. According to Thoma's view, this reaction of the intima is compensatory and adaptive, tending to strengthen the wall in the spots where it is weak and to restore the original lumen of the vessel.

Despite much discussion the following changes are still unsettled. Where does the process begin? Is there a true hypertrophy of the muscle fibres? What is the relation of high tension (hyperpiesis) to the sclerosis? Which comes first? Is the primary mischief caused by the action of a toxin in the finer tissues of the capillaries and arteries? Or do these irritating substances cause spasm of the smaller vessels, and so raise the tension? What is the relation of the involutionary changes in the vessels in old age to those met with in younger persons? May not increased viscosity of the blood play an important rôle in causing high tension and arterial strain? The whole subject is in the melting pot again in consequence of the remarkable studies on experimental arteriosclerosis. We lack definite knowledge of the finer changes in the capillaries, which are probably always involved (as Gull and Sutton believed), through which, after all, the essential processes of the circulation are carried on. As age advances the smaller vessels show definite changes, chiefly in thickening of the intima and moderate hypertrophy of the other coats. Later, degeneration occurs, fatty and necrotic, particularly to the muscle cells and in the elastic fibres of the media, and calcification is common. Alterations precisely similar to this physiological arteriosclerosis may be met with in young persons, even in children, and it is pathological only in the time of life at which it has occurred. Intimal thickening in which both the elastic and connective tissue elements are concerned is perhaps the most constant feature in all types of arteriosclerosis. It may be out of all proportion to the changes in the media, and may narrow or obliterate the lumen of the vessels—*endarteritis obliterans*. This is the most important single factor in the disease, responsible for more symptoms than all the other changes put together. It may be limited

¹ *Arch. Int. Med.*, 1920, **26**, 38; and 1923, **31**, 653.

to one set of vessels, as of the legs or of the heart. The cause of this intimal thickening is much discussed. Thoma regards it as compensatory, particularly in the large vessels, but even in vessels the size of the ophthalmic artery he thinks it takes place to strengthen the vessel at a point weakened by disease of the media as illustrated in his well-known figure.¹ (See Fig. 95, p. 848.) The physiological intimal thickening as age advances is believed to strengthen the vessel weakened by senile changes in the elastic and muscular elements of the media, and in the pathological forms experimental evidence is in favor of this view.

The nature of the changes in the media and adventitia are much discussed. They probably differ in the different groups of cases. In the high tension—hyperpietic—form there appears to be an early hypertrophy of the muscular elements. It is not easy to determine this histologically, and the matter is still in dispute. The cut section of an artery contracted is very different in appearance from one relaxed, and appearances are very deceptive. This has been well pointed out by Arthur V. Meigs, whose figures of cross-sections of shrunken and unshrunken arteries show how different the coats look in the two states. In the involutionary and toxic forms, necrosis of the muscle fibres and elastic elements takes place with replacement by connective tissue, fat, or lime salts, very much as occurs in the larger vessels. The medial degeneration seems really as important in the small as in the larger arteries, and in the senile type the calcified beadings follow these necrotic changes.

Symptoms.—Arteriosclerosis disturbs function in three ways: (1) Following progressive arteriosclerosis the activity of an organ lessens and there is a gradual reduction in its capacity for work. The changes of senility are largely vascular. With a reduced blood supply the organs become less and less active, atrophy slowly but progressively comes on, and they become firmer and harder. In old age every organ and tissue in the body shows changes which may be attributed to progressive arteriosclerosis. (2) When the arteriosclerosis reaches a final and obliterative stage, if in an end vessel, atrophy follows in the territory supplied as in the arteriosclerotic kidney, or if, as so often happens, it is in the peripheral vessels of the foot or of the hand, gangrene supervenes. (3) Arteriosclerosis renders the small arteries more prone to spasm than normal vessels. The process may sometimes be studied in the vessels of the leg. The spasm is accompanied by pain, ischemia, and loss of function. The diminished volume of the pulse is readily perceptible, the foot becomes pale, at the same time there is pain, and, if at all widespread, there is muscular disability. These attacks of angiospasm are not necessarily associated with sclerosis. Vascular crises have been introduced to do service in explanation of a whole series of phenomena, from lead colic to angina pectoris, and from cramp of the muscles to the gastric crisis of tabes. Pal, of Vienna, in his monograph on *vascular crises*,² gives an excellent account of the whole condition. He refers to a case of great importance as illustrating the loss of function in a part caused by transient spasm. A man, aged sixty-three years, every day,

¹ *Virchow's Archiv.*, 1888, **111**, 76.

² *Gefässkrisen*, Leipzig, 1905, p. 275 (S. Hirzel).

or every few days, had blindness of the right eye, lasting from a minute to several hours. Complete amaurosis with absence of pupil reaction was found. The ophthalmoscopic examination showed contraction of the retinal arteries and emptiness of the veins, which passed off in a few minutes with restoration of normal vision.

In so widespread a disease the clinical features will depend upon the extent to which the process has involved the arteries of different organs. So remarkable are the powers of adaptation in the body that an extreme grade may be compatible with good health. It is an every-day experience to find arteriosclerosis in persons who look well, and who are able to perform the ordinary duties of life. Sudden death may be the first and only manifestation. Rupture of a bloodvessel in the brain, thrombosis of one of the coronary arteries, rupture of a small aneurism, acute dilatation of the heart—any one of these may carry off a man in whom there has never been any suspicion of an organic lesion. Natural death, euthanasia, comes through the bloodvessels. The description in Ecclesiastes of the gradual failure of the vital powers is an epitome of the clinical features of senile arteriosclerosis. The symptoms are as varied as the organs involved. But before entering into consideration of the special features, it may be well to consider arteriosclerosis as a—

General Disease.—As already stated, there may be no symptoms of ill health, and the condition may be met with in a casual examination. In a man who has led a very energetic life, particularly if he has worked hard with his muscles, eaten much, and drunk hard, the palpable arteries are felt to be thickened, the blood-pressure is heightened, there is an increase in the vigor of the cardiac impulse, the apex beat is a little dislocated outward, the first sound is thudding and prolonged, and the second is accentuated. Such a patient may look a very robust man. When present under the fortieth year, such features are always of serious, although not always of immediate significance, and it does not do to give a too unfavorable prognosis. Mental and bodily vigor of exceptional degree may persist with the most pronounced arteriosclerosis. The discovery may be a most advantageous thing, as the patient may be warned to change his method of life. A man who has been in constant hazard of a breakdown may be able to keep up indefinitely when the pace is reduced. An early symptom of the general disease is a slight pallor, all the more noticeable if the individual has had previously a high color. With it there may be no actual reduction in the number of red blood corpuscles. A gradual loss of intellectual and bodily vigor is the most striking symptom. Within a few years a man may age visibly and lose his intellectual keenness. The muscular energy is lessened and he is prematurely senile. Often the skin gets flabby and lax and the hair turns gray early. Slowly advancing, the peripheral arteries harden, the retinal vessels become more tortuous, the blood-pressure rises to 150 to 200 mm. Hg., the cardiac hypertrophy becomes more marked, and the urine shows a slight amount of albumin and tube casts. Even at this stage the conditions may have been met with accidentally and the patient may be quite able to attend to his business, although conscious of failure in capacity. Very many of these patients, particularly under forty years,

come to us with symptoms of neurasthenia, irritable, sleepless, and emotional. A marked loss of weight is not uncommon.

Local Manifestations.—Nervous System.—As just mentioned, the patient may present quite early all the complex and varied manifestations of neurasthenia. In the more advanced stages of the disease the cerebrospinal features are among the most important and interesting. *Headache* is an early and distressing symptom, associated, as a rule, with high pressure and often promptly relieved by measures which reduce it. Usually frontal and continuous, occasionally paroxysmal and resembling migraine, many patients first consult a physician for it and the real cause may be overlooked, unless careful examination is made.

Vertigo.—Transient giddiness is a very common symptom and may be one of the most distressing, although it is usually quite temporary and never with the severity or associated features of Ménière's disease. It may, however, be associated with tinnitus. It is often brought on by exertion, or follows a sudden movement, and is an accompaniment of the crises of hypertension to which some patients are subject.

According to Stein¹ acoustic or vestibular phenomena (decrease of hearing, nystagmus and dizziness), may appear without any other symptoms referable to the circulatory apparatus. If complete deafness occurs, a serious anatomical lesion, as embolism or hemorrhage must be suspected.

Transient Monoplegias, Aphasia, and Paraplegia.—One of the extraordinary cerebrospinal manifestations is the occurrence of attacks of transitory disturbance of function of parts of the brain or of the cord, leading to hemiplegia, monoplegia, aphasia, or even paraplegia. Years ago the senior writer's attention was called to these occurrences in the case of a friend and colleague, a man of about forty years, with extreme arteriosclerosis. After an attack of slight palpitation of the heart, with shortness of breath, he awoke one morning to find himself unable to speak or to use his right hand. The paralysis passed away in the course of twenty-four hours, and he regained the power of speech a little more slowly. He had a dozen or more of these transient attacks, some lasting a little longer than others, but with recovery so complete that he was able to resume his work. Once there was transient paraplegia, and for more than two days he was unable to walk. Headache was variable, not always present. This is a not very uncommon feature in arteriosclerosis of the cerebral vessels. The attacks are sudden and the recovery is complete. One patient had, within two years at least twenty attacks of transient paralysis, sometimes on one side, sometimes on the other. Such attacks of intermittent closure of the cerebral arteries are almost always associated with a high blood-pressure. Although not so widely recognized as it should be, the condition has been described by many writers, particularly Peabody, Edgeworth, Phillips² and others. The transitory nature, with complete recovery and the extraordinary frequency of the recurrence, put hemorrhage, embolism, and thrombosis out of the question, and the condition must be an angiospasm similar to that which produces manifestations of Raynaud's disease, and intermittent claudication of the legs.

¹ *Ztschr. f. klin. Med.*, 1920, **90**, 88.

² *Cleveland Med. Jour.*, 1912, **11**, 639.

Convulsions of an epileptiform character may occur. In the absence of syphilis and of lead poisoning, convulsions occurring in middle-aged individuals should always excite the suspicion of arteriosclerosis. They are associated with high pressure, sometimes very high, and are often preceded by headache and giddiness.

Progressive Dementia.—Gradual failure of the mental powers is one of the commonest symptoms of cerebral arteriosclerosis. A man begins to take less interest in his affairs, grows careless and apathetic, the memory and judgment are at fault, the facial expression is dull, and, progressing month by month, at last the psychical powers are so reduced that the individual is in a state of dementia. Apart from syphilis, in which the dementia has the well-known features of paresis, mental degeneration is not often seen as a result of arteriosclerosis in men under forty years. It is common enough as a presenile change in men at or about sixty years. It may be associated, too, with periods of excitement and with mental vagaries of all sorts. Rupture of the cerebral arteries leading to apoplexy and thrombosis in consequence of changes in the intima are common events in arteriosclerosis.

Cardiac.—There are three important groups of cases in which the dominant symptoms of arteriosclerosis arise from affection of the heart—the valvular, the myocardial, and the coronary.

Valvular Group.—In a considerable number of aortic and mitral valve lesions the insufficiency is due to a process in the segments identical with that in the vessels. The former is a much more important group and a proportion of cases of aortic insufficiency in men belong to it.

Myocardial.—In general arteriosclerosis gradual failure of the hypertrophied cardiac muscle is a common and serious event, leading to the characteristic picture of myocardial insufficiency. After a period in which the patient suffers with palpitation or violent action of the heart, he begins to get short of breath and is winded quickly by the stairs or by a slight hill. He may awaken at night in a slight paroxysm of dyspnoea. At this period examination may show a forcible apex beat and a high-tension pulse. An attack of angina pectoris or of pulmonary oedema may occur. Soon the dyspnoea increases, the signs of dilatation of the heart become more marked, and there is a characteristic picture of orthopnoea, slight swelling of the feet, and cough, with, perhaps, blood-stained expectoration. The pulse at this stage is often very deceptive, as it is not always weak. The apex beat is diffuse, undulatory on palpation, and one may feel a gallop rhythm, while over the whole heart the gallop rhythm is heard on auscultation. There may be an associated systolic murmur, and the aortic second sound may still be ringing or even amphoric in tone. The state of the urine depends entirely upon the degree of venous congestion. With judicious treatment the condition may be relieved in a week or ten days, and the patient may be able to resume work. A dozen or more of such attacks may follow before the patient succumbs. Even after months of dyspnoea, recovery may take place.

Coronary Arteries.—The orifices, the main branches, or the smaller vessels may be affected. The narrowing of the orifices is a common cause of myocardial degeneration and weakness, and, in young syphilitic

subjects, of attacks of angina. The same may happen in any case in which the sclerosis is advanced at the root of the aorta and the orifices of the coronary arteries are seriously narrowed. Involvement of the main branches produces the same condition, but attacks of angina pectoris are more common and in a large group of cases sudden death occurs from thrombosis in one or other of the branches. In many instances of arteriosclerosis in comparatively young men the coronary arteries are involved out of all proportion to the other vessels and the attacks of myocardial weakness may precede or accompany angina pectoris, or one may be surprised to find, in a case of sudden death in a middle-aged man, who has never had any cardiac symptoms, that there is gradual fibrosis or perhaps areas of anemic necrosis are present with softening and occasionally rupture.

Pulmonary Artery.—Sclerosis of the pulmonary artery due to an infection by the *Treponema pallidum* has been described as "Ayerza's disease," whose main clinical feature is a marked cyanosis of the face (hence the term "black cardiacs"). Postmortem there are secondary changes in the bronchi and lungs.¹ This symptom-complex must not be confused with that of polycythemia hypertonica as described by Geisboeck and Parkes Weber,² in which there is renal or primary arteriosclerotic hypertension with secondary polycythemia rubra. This in turn is distinguished from the true erythremia of Vaquez and Osler by the absence of splenomegaly and the presence of marked hypertension.

Renal.—There are two great groups of cases: (a) associated with the small contracted kidney, following an acute nephritis or coming on insidiously in gout or chronic lead poisoning, there is an extreme grade of arteriosclerosis which may be regarded as secondary and due partly to the high pressure and partly to toxemia; (b) the true arteriosclerotic kidney is a red, beefy organ which is firm, hard, and dark in color, not at first reduced in size, sometimes, indeed, slightly enlarged. Very often, with this kidney, there may be few or no urinary symptoms. In a late stage there may be large, flat areas of atrophy of the cortex, or a large section of one organ may be involved in consequence of an obliteration of the arteries passing to the part.

The *urine* in these two groups of cases present, as a rule, striking differences. In the small contracted kidney the amount is increased, the specific gravity is very low, the albumin small in amount, often absent in the morning, hyaline casts are present, and very often red blood corpuscles. The urine of the arteriosclerotic kidney may contain at first no albumin, or, if present, the amount is not large, the specific gravity is normal or sometimes high. Later, the albumin may be large in amount and sometimes, as when a patient is admitted with an attack of cardiac dilatation, the urine is scanty with large amount of albumin and numerous tube casts, due to an acute intercurrent nephritis.

Abdominal.—Much attention has been paid of late years to abdominal symptoms in arteriosclerosis. Pal and others believe that very many of the painful gastric and intestinal conditions are associated with spasm

¹ *Rev. Assoc. méd. argent.*, 1924, **37**, 110.

² *Proc. Roy. Soc. Med.*, 1925, **18**; *Clin. Sect.*, 37-38.

in the gastric and mesenteric vessels; some would associate the multiple functional disturbances of abdominal neurasthenia with degenerative changes in the arteries. Certainly one may see a sclerosis of the mesenteric vessels far in advance of that in other vascular territories, but it is doubtful if we are yet in a position to say that any definite symptoms are connected with it. Ulcer has been met with in connection with endarteritis of the smaller vessels of the stomach. The victims of angina pectoris may have marked abdominal symptoms, and writers have spoken of such attacks of abdominal pain as *angina abdominis*. This is really an old story, as years ago Leared described "a disguised disease in which the heart affection was so masked by that of the stomach that nothing in the statements of the patient had any bearing on the primary disease." Even when the pain is entirely abdominal the general features are usually sufficient to make a diagnosis.

Milder attacks of epigastric pain and intestinal cramp and meteorism have been attributed to arteriosclerosis. The clinical features of gastric and intestinal dyspnoea have been regarded as manifestations of circulatory disturbance in the sclerotic vessels. One cannot read the literature on the subject without feeling that the writers have often been carried away with theoretical considerations. An intermittent claudication of the stomach has been described.

Peripheral Arteries.—A few among the many manifestations following sclerosis of the arteries of the limbs may be considered:

Cramps of the Muscles.—Local tetanus (cramp) in a muscle follows overexertion or a sudden prolonged effort in a strained or unaccustomed position. Long-distance runners are very subject to cramp in the calves of the legs, and sustained use of any group of muscles may throw not the whole group, but some portion, into strong tetanic cramp. This form and the commoner variety, which results from strained posture, are met with in young and old, but in the latter there is a form of great interest, and often very troublesome, which is probably associated with arteriosclerosis. Few elderly persons escape attacks of cramp, chiefly nocturnal and sometimes of such severity that the condition requires treatment. It is more common in persons who eat too much and work too little; but attacks may occur in thin, abstemious persons. It is difficult to connect the condition definitely with angiospasm, but the senior writer so often found marked sclerosis of the palpable vessels of the legs or absence of the pulse in the dorsal arteries of the feet, that he came to regard the bad nocturnal attacks in elderly persons as a manifestation of endarteritis. Twice attacks of the most dreadful agony have been seen, recurring every few minutes in the muscles of the legs, knotting them in places into hard lumps which took a minute or two to disappear. In one old woman they were so severe that only large doses of opium gave relief. In both these patients the pulse could not be felt in the feet. Ligation of an artery may throw the muscles into a spasm, and the sudden tap on the facial artery may cause tetany of the muscles, so that it is not impossible that angiospasm (a vascular crisis) may be responsible for these painful cramps in elderly persons.

Neuritic Pains—Erythromelalgia.—In connection with endarteritis obliterans of the vessels of the legs, numbness, tingling, burning, and shooting pains are common complaints. In diabetes a whole group of neuritic symptoms may precede the local gangrene of the toes, and the same may occur before senile gangrene. In erythromelalgia, arteritis obliterans has been found. There is a very interesting group of cases of idiopathic endarteritis of the vessels of the legs, in which in comparatively young men, without any evidence of syphilis, pains precede the occurrence of the severe obstructive manifestations.

Intermittent Claudication.—In the cases in the horse, described by Bouley, and in Charcot's original case in man, the vascular obstruction was aneurismal. To Erb we owe the recognition of the frequency of this symptom in arteriosclerosis of the vessels of the legs. It is a question of a due balance between a supply of energy through the blood and muscular expenditure, as Allan Burns puts it in his original explanation (1809). There are cases with neuritic pains and well-marked signs of vascular disease, palpable vessels, spasm of the arteries, with pallor of the feet in exertion, or absence of pulsation in the dorsal arteries of the feet. In others, the signs of arterial disease are not so clear, and it is possible that there may be an angiospastic form; or it may be in some cases an affair of the spinal arteries with anemia of the cord. In the majority of the cases seen by the senior writer, the arteriosclerosis has been pronounced. It is not always a cramp-like pain that causes the limping or claudication, but there may be a relaxation of the limbs, a giving way for a few seconds, or, without actual falling, an inability to make any further effort.

Diagnosis.—To the rule that the disease is uniformly distributed in the body there are many exceptions. The most widespread peripheral arteriosclerosis may exist with a moderate grade of disease of the aorta. On the other hand, the endarteritis deformans of the latter vessel may be out of all proportion to the disease in the smaller arteries. The vessels of the head, of the heart, or of the kidneys may be in an advanced stage of sclerosis, without any change in the palpable arteries. The most serious form is that in which the smaller vessels are chiefly affected and which comes on in middle life or in young persons.

From the appearance of the individual not much may be determined. To no condition is Shakespeare's remark more applicable—"the outward shows may be least themselves." A robust, vigorous looking man in the prime of life may have vessels in the most advanced stage of sclerosis. While there are patients who present a pronounced anemia, the florid cardiovascular facies is the more common. The active muscular business man of forty-five years, who all his life has never had to spare himself, and who has prided himself on his "fitness" for everything, is shocked to find that there is something wrong with the machine; or to the young-old man who has reached the grand climacteric without a day's illness, Nemesis whispers "time is up." In other instances a remarkable change takes place in a few months. Following, perhaps, a domestic shock or a financial crisis, in other instances without any obvious cause, a man begins to fail. The elasticity and firmness go from the gait, the

movements become less active, there is loss in weight, and the intellect is impaired. So rapid is the breakdown that some of these instances of presenile arteriosclerosis may be termed acute. Too much stress must not be laid upon certain features usually regarded as indicative of degeneration. Early graying of the hair may have nothing whatever to do with arteriosclerosis. Nor is the arcus senilis of much value as an indication. It may occur in middle-aged men with perfectly good arteries, and it does not seem to be a special feature in early arteriosclerosis.

The cardinal points in a case of arteriosclerosis are usually well marked: (1) thickening of the peripheral vessels; (2) signs of hypertrophy of the left ventricle, shown by the apex beat dislocated outward, the thudding first sound, and the accentuated aortic second; (3) heightened blood-pressure; (4) a slight and variable amount of albumin in the urine. In the senile form there is neither an increase in the blood-pressure nor cardiac hypertrophy. As a rule, this quartet of symptoms is present in a large proportion of the patients when first they come under our observation. At this stage the damage is done. The important point for the practitioner is to learn to recognize the early stages when there is a reasonable chance that the progress may be arrested. We can form a pretty clear judgment of the state of the arteries and the general physics of the circulation by sight, by touch, and by the study of the pulse.

When at all advanced, the superficial arteries of the body become visible and tortuous. This is particularly well seen in the temporals, which, as age advances, stand out as prominent, tortuous, even beaded cords. One must learn not to mistake a full for a sclerotic vessel. When the peripheral circulation is relaxed, as in high external temperatures or during excitement, the superficial arteries become prominent. When the sclerosis is at all advanced the brachials stand out markedly sinuous and throbbing visibly. The radials and ulnars, the external iliac just above Poupart's ligament, the femorals just below, and the dorsal arteries of the feet may all be visible. Of all vessels in which to see early thickening, the retinal arteries are the most important. de Schweinitz in particular has called attention to the great importance of its early recognition by the ophthalmoscope. Not only may it be readily seen that the arteries are thicker than normal and more tortuous, but the way in which they cut across the larger veins is very distinctive. A small hemorrhage may sometimes be seen.

By *palpation* we are enabled to judge with fair accuracy of the degree of thickening of the vessel wall. It requires not only experience, but education, to form a correct judgment on the state of the arteries. A perfectly normal vessel, when contracted, may feel hard and cord-like. On the other hand, in a radial definitely thickened, but in a state of extreme relaxation, the hardening of the walls may escape detection. The state of the tissues about the artery, the amount of fat in the skin, the size and fulness of the veins—all have to be considered. One of the commonest of mistakes is to regard as thickened any vessel one can roll under the finger. But in a state of very high tension and if very full, the arterial tube may feel cord-like. To estimate the presence of sclerosis it is not sufficient to examine the radials and temporals, but the brachials

and femorals should also be felt, and palpation should be made, first, in the natural condition; secondly, the artery should be felt below a point where the pulse wave is obliterated; and thirdly, a small section of the vessel should be emptied of blood and palpation made between the two points of pressure. It may only be in this last way that a true opinion can be formed of the existence of sclerosis. It does not do simply to obliterate the pulse and feel immediately below it, because the recurring pulse may appear beyond the point of pressure. In the superficial arteries, as the radial, the finger is able to appreciate four distinct grades: (1) The normal vessel wall, which in a moderately thin wrist may be first differentiated from the adjacent tissues; in the cold, or if the hand has been placed in ice-cold water the tightly contracted artery may be felt as a fine cord; (2) moderate sclerosis in which the vessel is readily felt and in which, after the blood has been pressed out of the artery, there is a definite tubular cord; (3) extreme sclerosis in which the radial is felt like a piece of whipcord, firm, hard, incompressible, rolling under the finger, and presenting little or no difference in the sensation with the blood in or out of the vessel; (4) calcification, which in the radial is easily felt, ringed or beaded.

According to Evans¹ the only adequate clinical evidence of diffuse hyperplastic sclerosis is a persistently raised systolic pressure of 190 mm. Hg. Early in the disease, or before the thickening of the vessel is evident, the blood-pressure may be persistently high. This *presclerotic stage* is important to recognize, and yet it is only exceptionally that we are able to trace all the stages in a given patient. More commonly the high pressure and sclerosis are coexistent, but there is no definite parallel between the two processes. The very highest pressures, above 250 mm. Hg., may be present with quite moderate thickening of the vessels. On the other hand, low blood-pressures may coexist with early arteriosclerosis, or following an acute illness, dilatation of the heart, a shock, or certain complications, such as pulmonary oedema, and in the late stages of the intercurrent affections.

The character of the *pulse* in arteriosclerosis is best described as hard and resistant, and the vessel is plainly perceptible to the finger in the intervals of the beats. As already mentioned, it is important to recognize the difference between the hard sensation conveyed to the finger by a high-tension pulse and that conveyed by stiffening of the walls. The two may coexist, but the former may give the deceptive sensation of a permanent cord to the artery. Usually, too, the pulse is incompressible, or, more correctly, is difficult to compress. One can always obliterate the pulse wave in the radial, but it quite commonly happens that, in spite of the firmest pressure, the pulsation may be felt beyond the finger. This is a recurrent pulse and may be checked by compressing the ulnar artery. It is present frequently in high tension, but it is just as common when the smaller arterioles are greatly relaxed and the peripheral tension low. To estimate the state of the vessel wall in a high-tension pulse, obliterate the radial artery close to the metacarpal bone, then with the

¹ *Quart. Jour. Med.*, 1920, **14**, 215.

index finger of the other hand press the blood out of a section of the radial, compress it, and then, with the middle finger, feel the empty vessel. If very sclerotic, it will be almost as prominent empty as full. But when the cord-like sensation is due to a high pressure only, there may be very little sensation given to the finger by the vessel wall itself. The tracing of the high-tension pulse is very characteristic, with a wave of moderate height, a sloping ascent, and a delayed decline with a little or no dicrotic wave. The measurement of the pulse-wave velocity by means of the hot-wire sphygmograph affords, according to Bramwell and Hill,¹ direct objective evidence in the diagnosis of arteriosclerosis.

Treatment.—Once degeneration, fibrosis and calcification have taken place, the damage is irreparable, and all the hygienic, dietetic, and medicinal measures cannot restore the normal structure of the arteries. But this does not mean that the condition is always hopeless. Much may be done to prevent the sclerosis increasing and much may be done to relieve symptoms.

The treatment may be carried out along the following lines, varying, of course, with the individual cases:

General.—The patient should be urged to live as peaceful a life as possible, cutting off all sources of mental strain and worry. A protracted holiday may be most helpful. It is not wise, as a rule, to urge a man to give up work entirely. Too often this is followed by a neurasthenic breakdown. The most difficult part of the treatment is so to arrange a man's life that he may have moderation in work. So long as it can be lightened, there is no reason why he should not continue. Of course, when there are signs of cardiac failure or any pronounced local features, or if the mental changes are marked, it would be wise to urge complete rest. These patients often require the consolation of sensible advice. On hearing that they have hardening of the arteries, many men with years of useful life before them are inclined to throw up the sponge at once. When of moderate extent in a man aged forty-five or fifty years, it may not lessen the expectation of life by more than five or six years.

Exercise.—Golf, horseback riding, walking, bicycling, all in moderation, are advantageous. Allbutt recommends cautious hill climbing. The relaxation of the vessels of the skin and of the peripheral arteries generally which follows moderate exercise lowers the blood tension and relieves the heart. All sudden effort likely to throw a strain upon the vessels should be avoided. The action of the skin should be promoted by a daily bath. In the winter it is best taken at night and warm. An occasional Turkish bath, with a good rub, is helpful.

Food.—The one essential factor in the diet of arteriosclerotic patients is reduction in the amount. He should be taught gradually to reduce the quantity of food until he finds the minimum on which he can maintain the mental and bodily vigor. He will often be surprised to find that it is one-third or one-fourth of that which he has been in the habit of taking. He may take a cup of tea, a boiled egg, and a couple of slices of toast for breakfast; a vegetable soup with a rice pudding for luncheon; a piece

of fish, a couple of vegetables, and stewed fruit for dinner, with a glass of hot milk at night, or a bowl of bread and milk. With a diet along these lines an arteriosclerotic may successfully pray the prayer of Hezekiah, and get, like him, a fifteen years' extension. He can do without meat perfectly well. Oysters, eggs in moderation, and fish may be taken with plenty of fruit, vegetables, plenty of bread and butter, and milk. It does not seem that we need dread specially the injurious effects of the lime salts which are abundant in milk and in eggs. Buttermilk is an excellent and easily digested food, even when milk is not. Sour milk has been a favorite drink with many persons who have lived to a very advanced age, like Thomas Parr. Spirits of all sorts should be given up. Tea and coffee may be taken in moderation. A man who has been a heavy smoker should reduce his allowance to two or three cigars a day.

Removal of Toxins.—Any possible source of these should be remedied. The mouth should be carefully examined, any defective teeth being remedied or removed and pyorrhœa alveolaris rigorously treated. Inquiry should be made for syphilis and special treatment given if necessary. A Wassermann test would eliminate those cases certainly due to syphilis.

Medicinal Treatment.—Of remedies believed to have an influence directly upon the coats of the vessel, only iodide of potassium is of value. It is stated that, experimentally, arteriosclerosis may be prevented if, coincidentally with epinephrine, iodide of potassium is given to the animal. In all syphilitic cases it should be used freely, and even in the early stages the drug should be administered in moderate doses, 5 to 10 gr. (gm. 0.3 to 0.6) three times a day, and kept up for some months.

The blood-pressure is more influenced by dieting and mode of life than in any other way. Of the drugs which have an influence, the nitrites are the most important. The commonly used nitroglycerine is often effective, but rarely given in large enough doses, and even then is apt to be very transient in its effect. It is best given in solution freshly made, and the patient may take from 1 to 3, 4, or 5 minims of the 1 per cent. solution three or four times a day. In crises of high tension larger doses may be given. It does not seem to do any harm, and individuals react so differently to the drug, that it is well always to test it upon each patient. We often do not get good results until much larger doses are given than those usually employed. The sodium nitrite, in 1 to 4 gr. (0.06 to 0.25 Gm.) doses every three or four hours, has a somewhat more permanent action and is often of very great service. Erythrol tetranitrate in doses of gr. $\frac{1}{4}$ to 2 (0.015 to 0.13), has a still more prolonged action.

Arsenic in small doses is helpful, particularly in the cases with early anemia. In the crises of hypertension, brisk saline cathartics are most helpful. In any case it is well to bear in mind that the only valuable measures for permanent reduction of blood-pressure are the hygienic and dietetic. The treatment of the various complications of arteriosclerosis are dealt with in the other sections on diseases of the heart, kidneys, etc.

POLYARTERITIS ACUTA NODOSA (PERIARTERITIS NODOSA)

In 1866, Kussmaul and Maier reported a case of a man, aged twenty-seven years, who had an acute, progressive "chlorotic marasmus" with fever and tenderness of the skin and muscles. Hard, bead-like nodules were present in the skin of the thorax and abdomen, which were afterward found to be thickening of the subcutaneous arteries. The case was thought to be one of trichinosis. Postmortem, little aneurisms were found on almost all of the smaller arteries of the body. These were believed to be due to inflammatory infiltration of the adventitia, and they gave the name *periarteritis nodosa*. Since then 82 other cases have been recorded. The most important contributions are those of Dickson,¹ Lamb,² Klotz,³ Harris and Friedrichs,⁴ and Ophüls.⁵ It is a disease chiefly of the male sex, and of the third and fourth decades of life, as the ratio of the male to female cases is 5 to 1, and the average age is thirty-one years.

The arteries of the heart, the kidneys, mesentery, and the liver were attacked in all the cases.

Dickson and Klotz state that there is a primary periarteritis established, involving the vasa vasorum and accompanied by a hyaline degeneration of the media. The earliest lesion apparently is a destruction of the muscular coat with a giving way of the internal elastic of the adventitia leading to aneurismal dilatation. The resulting injury to the tissues or organs is represented by various retrograde changes "attributable to the curtailment of blood supply by thrombosis or to pressure injury from hemorrhagic extravasation." Cloudy swelling, fatty degeneration, coagulation, necrosis, ulceration or other form of cell destruction are observed, hence the hemiplegia, myocarditis, nephritis, ulcerative enteritis, etc., which are so frequently found. While syphilis is excluded even as a predisposing factor the case for various bacteria and even for a filterable virus is still not proved. Yet most authorities are agreed that periarteritis nodosa is a specific infection *sui generis*, as suggested by the following facts. First, that a similar pathological entity occurs in epidemic form in stags; secondly, that successful transmission experiments have been reported.

The physical features depend a good deal upon the vessels affected. The onset is, as a rule, sudden and there is moderate fever throughout. Weakness, hyperesthesia, pains in the muscles, anesthesia, and anemia are marked symptoms. Vomiting and diarrhoea are common. Leukocytosis is constant and varies from 11,000 to 30,000. Various skin eruptions have been noted as erythema, urticaria and purpura. Several cases have shown albuminuria, hematuria, cylindruria and the picture of an acute nephritis. When the coronary arteries are affected the picture is of myocardial insufficiency, rarely in association with anginoid pain. When the peripheral arteries are involved the main symptoms are cramps and wasting of the muscles, painful joints, and very occasionally palpable

¹ *Jour. Path. and Bact.*, 1908, **12**, 31.

² *Jour. Med. Res.*, 1917, **37**, 1.

³ *Arch. Int. Med.*, 1923, **32**, 870.

⁴ *Arch. Int. Med.*, 1914, **14**, 481.

⁵ *Ibid.*, 1922, **43**, 285.

nodules in the subcutaneous arteries. Headache, excitement, convulsions, optic neuritis, and paralysis may be present when the cerebral vessels are involved.

The diagnosis has rarely been made, in fact in only 4 cases; the condition is usually mistaken for meningitis or typhoid fever. A remarkable case was admitted to the senior author's service and is reported by Sabin:¹ The patient was a woman, aged thirty-two years, who had had dilatation and vomiting with emaciation and areas of anesthesia; she looked very ill and had been confined to bed for five weeks. There was an extreme grade of annular sclerosis of the arteries; numerous subcutaneous hard nodules were scattered over the abdomen, just such as were present in the case of Kussmaul and Maier. The case was very similar to the one reported by H. M. Fletcher.²

The *treatment* is purely symptomatic and consists largely in supporting the patient's strength and making him comfortable. This implies rest, a nourishing and digestible diet, iron and arsenic for the anemia, and normal saline and blood transfusions for the toxemia.

THROMBO-ANGITIS OBLITERANS

Synonyms.—Buerger's disease; endarteritis obliterans; endarteritis productiva; spontan gangraen; die hebraische krankheit; arteriosclerotic gangrene; presenile and juvenile gangrene.

Etiology.—Among the predisposing factors are race, age and sex. As Buerger³ pointed out the Hebrew race is especially prone to the disease as there were only 10 Gentiles in his series of 500 cases; other authors however have reported an identical symptom-complex in the Japanese (Koga⁴), Chinese (Whyte, Meleney and Miller⁵), the Swedes (Ochsner⁶) and the Anglo-Saxons (Telford and Stopford⁷); the junior writer has seen one case in an Irish-Canadian. It is essentially a disease of the fourth decade, the average age in Buerger's series being thirty-two years and five months, but it has occurred in both younger and older subjects, the extremes ranging from seventeen to fifty-six years. The male seems much more susceptible as Buerger has only 3 women among his 500 cases. Tobacco is regarded as a predisposing factor because the majority of the patients are heavy cigarette smokers; possibly the nicotine causes some alteration in the wall of the vessels that renders them more liable to the attacks of inflammation and thrombosis. Syphilis plays no important role, as repeated Wassermann tests of the blood of these patients have proved invariably negative. W. Meyer⁸ believes that *hyperglycemia* due to some endocrine disturbance is the underlying fault and suggests naming the disease "glycophilia." He also noted an increase in the number of erythrocytes and blood platelets and believes that the thrombi are really a conglomeration of red blood cells due to erythrocytosis and

¹ *John Hopkins Hosp. Bull.*, 1901, **12**, 195.

² *Beitr. z. path. Anat.*, 1892, **11**, 323.

³ *The Circulatory Disturbances of the Extremities*, 1924, p. 213. (W. B. Saunders & Co.)

⁴ *Deutsche. Ztschr. f. Chir.*, 1913, **121**, 371.

⁵ *Ann. Surg.*, 1925, **81**, 976.

⁶ *Surg. Gyn., and Obst.*, 1915, **21**, 536.

⁷ *Brit. Med. Jour.*, 1924, **ii**, 1035.

⁸ *Jour. Am. Med. Assn.*, 1918, **71**, 1268.

stasis. The majority of observers, however, are in accord with Buerger who regards infection from some unrecognized bacterium or ultra-microscopic virus as the exciting factor. While most observers have failed to identify a specific organism, Rabinovitch¹ claims to have isolated a medium-sized, motile, beaded and rod-shaped bacillus, having special reactions on sugars, and capable of reproducing the disease in rabbits; further confirmation of this work is not yet forthcoming.

Pathology.—The deep vessels, both arteries and veins, of the extremities but particularly of the lower extremities, reveal an acute inflammatory process in all the vascular coats as shown by a diffuse infiltration with leukocytes. This inflammation is followed shortly by an occlusive thrombosis; the vessel is found filled with a grayish or yellowish mass of thrombus merging into softer, more brownish and more recent clot, which terminates abruptly in the lumen of an apparently normal vessel. Certain miliary pus foci containing giant cells, endothelioid cells, leukocytes and disintegrated nuclei are found lying usually in the periphery of a red or mixed clot; these areas strongly resemble tubercles and suggest the presence of some specific toxin, or more probably a microbic agent. The artery or vein is usually contracted, so that its wall appears somewhat thickened. There is an associated periarteritis, which in some cases is so great that it binds together the veins, arteries and nerves; in other cases it is almost absent. In 20 to 25 per cent. of the patients the superficial veins of the arms and legs reveal a form of migrating thrombophlebitis. The latter may be present without involvement of the deep vessels. In chronic cases and in patients over forty years of age there may be some arteriosclerosis, but never to a pronounced degree.

In the healed or organized stage there is total obliteration of the artery and vein by connective tissue, containing many small vessels which become dilated and form large sinuses, canalizing the clot. The giant cell foci and the inflammatory products have disappeared. In the late stages of the disease gangrene of the peripheral parts, particularly of the terminal phalanges of the toes and fingers makes its appearance. There is little or no involvement of the periosteum and bone.

Symptoms.—*Onset.*—Vague pains in the sole of the foot or in the toes are often present for months or even years before the appearance of the more serious symptoms. The patient may consult an orthopædic surgeon for weak arches or flat foot. Others note coldness and numbness of the feet during cold weather. In the course of time, the patient notices lameness due to pain in the calves of the legs and in the feet after walking variable distances, the syndrome of so-called *intermittent claudication*; the left leg is usually first affected. Even at rest there may be severe, non-localizable shooting pains in the calf or foot with tender calf muscles. About the same time a peculiar blush of the skin of the foot when the limb hangs down is observed, which has been termed *erythromelia* by Buerger. This cyanosis is replaced by a definite blanching of the skin of the foot when the limb is elevated; Buerger has found that this blanching appears when the leg is elevated at varying angles from 90° to 180°. The

¹ *Surg., Gynec. and Obst.*, 1923, **37**, 353.

greater the angle necessary for the blanching to appear the better is the *angle of circulatory sufficiency*. Weber¹ has called attention to the pallor of the foot on passive movement of the ankle-joint (*Oehler's symptom*). At this stage a careful examination shows a definite diminution in the pulse volume of the dorsalis pedis or of the posterior tibial arteries.

Weeks or months later the appearance of hemorrhagic blebs on the skin around the toe-nails and sometimes patches of dry dead skin are noted. These trophic disturbances are usually associated with great increase in the pain, which may become so excruciating as to make the patient's life almost unbearable. At this stage there is usually great tenderness along the calf and anterior tibial muscles. Peculiar subcutaneous nodosities may be found along the vessels of the leg and thigh. These are due to the superficial *migrating phlebitis* which occurs in some 20 to 25 per cent. cases. The fingers and hands may also be affected either with the first attack in the legs or subsequently. It is surprising how often one notes a diminution in the size of the pulse at the wrist long before the patient has noticed pain or change in the color of the fingers. Extensive gangrene of the fingers may occur without premonitory symptoms; in some cases extensive atrophy of the arm and forearm and even changes simulating scleroderma and sclerodactyly may develop. The roentgen-ray shows little or no change in the bones of the phalanges in marked contrast to Raynaud's disease and sclerodactyly, in which there is an absorption of the terminal portion of the affected phalanges. Of course after prolonged gangrene and infection there are some secondary destructive bony change from erosion and absorption. Intense mental depression is common and sometimes results in suicidal attempts. Atrophy of the leg and more rarely of the thigh muscles in varying degree is not uncommon, particularly when there has been occlusion of the popliteal or femoral artery for some time. A slight œdema may be present over the toes when there is some ulceration or gangrene in the neighborhood. In other cases there has been a chronic proliferative process in the subcutaneous tissues giving an appearance to the toes and foot as though they had been moulded in wax.

Buerger noted in one case incoherence of speech suggestive of some cerebral arterial lesion. Many of the patients develop epigastric distress or even excruciating cramp-like pains in the upper abdomen according to Schragar.

Diagnosis.—In a young male, and particularly a Hebrew, vague pains about the foot, painful cramps in the calves following exertion, cyanosis and ischemia of the foot with absence of the pulse in the dorsalis pedis artery would justify a tentative diagnosis, at least, of Buerger's disease. *Raynaud's disease* may give some difficulty, but is more likely to occur in women of eighteen to thirty years of age, who have received some psychic trauma or been exposed to severe cold. Further the attacks are periodic and very sudden in their onset, manifested by local syncope (pallor) followed shortly by local asphyxia (cyanosis) of the fingers in association with pain, paresthesia and anesthesia, but of comparatively short duration. Between the attacks the parts affected return to normal, though there may result marked trophic ulcers, and even gangrene. Further the

¹ *Quart. Jour. Med.*, 1916, 9, 289.

roentgen-rays show atrophy of the ends of the distal phalanges similar to that in sclerodactyly.

Erythromelalgia affects older people and usually males, and is generally confined to the feet, which are painful, hot and flushed, particularly during the warm weather. In both these conditions the peripheral arteries can be felt to pulsate. Gangrene of arteriosclerotic origin whether complicated by diabetes or not, should give no trouble.

Prognosis.—The course varies greatly; some have mild symptoms for years; others present a more acute fulminating variety ending in gangrene, necessitating bilateral amputation. In the majority of cases, however, the course is chronic, lasting ten years or more, with alternating periods of remission and relapse. Parkes Weber¹ reported a case of twenty-two years' duration. It may end fatally when some important vessel such as the renal, coronary (Perla²) or other large visceral artery is attacked. The cause of death is generally an intercurrent infection.

Treatment.—The palliative measures consist in absolute rest with the application of superheated air, either by baking or Bier's suction cylinders. Others advise exposure to the quartz lamp or the ultra-violet ray. Philips and Tunick³ recommend deep roentgen-ray therapy at weekly intervals. Electrotherapy has not much effect. Buerger feels that postural methods and passive movements to promote circulation in the limb are of more use than any of the above procedures.

The administration of the various drugs, as nitroglycerine and potassium iodide is scarcely worth while. Many have recommended hypodermoclysis with Ringer's solution (400 to 500 cc.) daily for three or four weeks in the belief that the viscosity of the blood will be diminished (Mayesima-Koga).⁴ Meyer has given 8 to 10 quarts of this solution daily by the duodenal tube with this end in view. Because of the increase in coagulation time intravenous injection of moderate amounts (250 cc.) of 2 per cent. sodium citrate has been tried.

Locally the ulcers should be treated with balsam of Peru or scarlet red ointment.

Of the various *surgical palliative measures*, ligation of the proximal end of the femoral vein is recommended by Ginsburg. Arterio-venous anastomosis is not as a rule possible as the veins are rather extensively diseased; if, however, the superficial and deep veins are patent (and particularly the internal saphenous and its tributaries) and there is a good pulsating femoral artery, the procedure may be tried. While periarterial sympathectomy may be indicated in Raynaud's disease, it is difficult to conceive how the advanced thrombus occlusion of the bloodvessels in Buerger's disease can be influenced by section of the vasomotor fibres of the sympathetic nerves. The results have not been satisfactory.

Amputation for ischemia or even gangrene is only justifiable after first trying conservative methods, but may be inevitable. Surgeons are becoming more and more conservative in this regard, although the patient often pleads for amputation to obtain relief from pain.

¹ *Proc. Roy. Soc. Med.*, London, 1925, **18**, Clin. Sect., 38.

² *Surg., Gynec. and Obst.*, 1925, **41**, 21.

³ *Jour. Am. Med. Assn.*, 1925, **84**, 1469.

⁴ *Mit. a. d. Grenzgeb. d. Med. u. Chir.*, 1912, **24**, 413.

CHAPTER XXIII

ANEURISM

BY THE LATE SIR WILLIAM OSLER, BART., M.D., F.R.S.

REVISED BY

CAMPBELL P. HOWARD, M.D., C.M.

Definition.—A tumor containing blood in direct connection with the cavity of the heart, the surface of a valve, or the lumen of an artery.¹

Classification.—It is not easy to make a satisfactory division of the various forms of aneurism. The following will be found a useful one for practical purposes:

1. *True aneurism* (A. verum, A. spontaneum), in which one or more of the coats of the artery form the walls of the tumor.

(a) *Dilatation aneurism.*

1. Limited to a certain portion of a vessel—fusiform aneurism, cylindroid aneurism.

2. Extending over a whole artery and its branches—cirroid aneurism.

(b) *Circumscribed saccular aneurism*—the common form in the aorta in which there is distention of two or more of the coats, or of the adventitia after destruction of the intima and media.

(c) *Dissecting Aneurism*, with splitting of the coats to a greater or less extent and occasionally with the formation of a new tube lined with intimal endothelium.

2. *False aneurism*, following wound or rupture of an artery, causing a diffuse or circumscribed hematoma.

3. *Arteriovenous aneurism*—communication between artery and vein, either direct—aneurismal varix—or with the intervention of a sac—varicose aneurism.

4. *Special forms*, such as the traction aneurism, the erosion and parasitic forms, which have a pathological rather than a clinical interest.

Etiology and Pathology.—**Incidence.**—That the number of aneurisms differs in different localities has long been recognized. Lucke and Rea² in a study of statistics found 1 case of aneurism in 41 autopsies in the United States (16,200 autopsies); 1 in 74 in Great Britain (36,500 autopsies); 1 in 109 in Scandinavia (5490 autopsies); and 1 in 111 in Germany and Austria (160,145 autopsies). According to Boyd³ it is responsible for from 0.1 to 0.5 per cent. of deaths in American cities.

¹ It is not possible to frame a definition to include every condition which we now speak of as aneurism. For example dilatation of the aorta, the uniform enlargement of arteries of the third and fourth dimension, and the abnormal communication between vessels are not within this definition.

² *Jour. Am. Med. Assn.*, 1921, **77**, 935 and 1923, **81**, 1167.

³ *Am. Jour. Med. Sci.*, 1924, **168**, 654.

Age.—The large statistics of Crisp, 555 cases of aneurism in different situations, show the greatest frequency to be between the ages of thirty and forty years, 198 cases; between forty and fifty, 129. The incidence of the disease is below the age at which arteriosclerosis is met with. Of the 898 deaths from aneurism in males in England and Wales in 1905, 462 occurred between the thirty-fifth and fifty-fifth years. It may occur at any age. Le Boutillier¹ found in the literature 80 cases in persons under twenty years of age; only 14 were under twelve years of age, and the youngest was in a child of two. Eighteen of the cases were of the thoracic aorta, 5 of the abdominal. In the very young, congenital syphilis plays an important part, as in the remarkable case reported by Wilson and Marcy,² in a child aged four years with extensive arterial disease and a large aneurism of the arch of the aorta. Richey,³ however, states that the common exciting factor of aneurism in the young is the streptococcus viridans, and that syphilis played a minor role in the series of 42 cases analyzed by him. In the peripheral vessels the aneurisms are often of embolic origin. In extreme old age latent aneurism is not uncommon.

Sex.—The ratio of males to females is about 5 to 1. In Boyd's collected cases there were 3403 males and 606 females, a ratio of 5.6 to 1.

Occupation.—Hard workers, the strikers in foundries, the dock workers, soldiers, sailors, and the very muscular and robust men are chiefly affected, but the disease may occur in feeble individuals. For years it has been known that soldiers were peculiarly liable to the disease, and the studies of Myers, Welch, and others called attention to the great frequency of aneurism in the British army.

Race.—The Anglo-Saxon is stated to be more subject to the disease. In the United States of America aneurism is common among the working classes. It is more frequent among the negroes of the Southern States. In the wards for colored patients at the Johns Hopkins Hospital arterial disease and aneurism were relatively much more common than in the wards for the whites.

Determining Causes. The determining causes of aneurism of the aorta are three: First, poisons which lead to changes in the coats of the vessel; second, conditions which increase and keep up the arterial tension; and third, internal trauma, the strain of muscular effort, particularly in the fourth decade, when the vital rubber begins to lose its elasticity.

Among the most potent poisons in causing arterial changes are those of the acute infections, and among these the first rank is taken by *syphilis*. Someone has well remarked that "Venus loves the arteries." The older writers, particularly Paré, Lancisi, and Morgagni, knew of the close association of lues and aneurism. Among modern writers the connection was referred to incidentally, but it is only comparatively recently that investigations have shown the remarkably high percentage of syphilis among subjects of the disease. In his well-known investigation,⁴ Francis H. Welch, of the British army, found that 66 per cent. of his series had

¹ *Am. Jour. Med. Sci.*, 1903, **125**, 778.

² *Jour. Am. Med. Assn.*, 1907, **49**, 15.

³ *Arch. Int. Med.*, 1923, **31**, 232.

⁴ *Medico-Chirurgical Transactions*, London, 1876, **59**, 59.

had syphilis. He described very clearly, too, the macroscopic changes in the aorta, particularly the cicatricial-like puckering of the intima. It is notorious that a history of infection, even in persons with well-marked signs of the disease, is not easy to get, particularly in women. There are a great many cases in which syphilis is latent, but the more closely the question is looked into the more one becomes impressed with the importance of lues as the essential factor in the causation of aneurism in persons under forty-five years of age.¹

Many studies have confirmed the view that the primary change is in the media, and there is now very generally recognized a *syphilitic aortitis* with definite characteristics. Macroscopically, it may be limited in extent, localized at the root of the aorta, or about the orifice of an aneurism, or there is a band of an inch in width on some portion of the tube, while other parts of the aorta and its branches are normal. In other instances the intima is involved, not with the usual plaque-like areas of atheroma, but there are shallow depressions of a bluish tint and short transverse or longitudinal puckerings, sometimes with a stellate arrangement; or the intima is pitted and scarred with small depressions and linear sulci. Microscopically the most important changes are found in the media and adventitia: (a) perivascular infiltration of the vasa vasorum; (b) small-celled infiltration in areas of the media, with (c) splitting, separation, and destruction of elastic fibres and the muscle cells. The process is largely a productive mesaortitis, and so marked may be the foci in the adventitia and media that they look like miliary gummata, and, in fact, were so described as far back as 1877 by Laveran and by Heiberg. The intima over these areas may be perfectly normal, but it often shows signs of thickening with fatty degeneration and the production of hyaline. Similar changes have been described in the larger bloodvessels in cases of congenital syphilis by Weissner, Bruhns, and Klotz.² And lastly, the specific nature of this mesaortitis has been determined by the detection of the *treponema pallidum*.

The experimental production of aneurism bears out this view. The high pressure caused by injection of epinephrine produces a fracture and separation of the elastic fibres of the media, and over these areas where the wall is weakened the intima may split with the formation of a localized aneurism, sacculated or dissecting, or the intima may gradually yield without actual rupture. The part played by the lymphatics in disseminating the luetic virus is emphasized by Klotz.³ He considers that the regions of the aorta most commonly affected by syphilis have the richest lymphatic supply. He frankly admits that it is not yet clear why and in what manner the virus finds its way to the thorax: "it is probably bound up with the question of the biological properties of the microorganism and the favorable conditions presented by particular tissues for its growth."

The following are among the important features of syphilitic aneurism: It occurs, as a rule, in persons under forty; the ascending arch is most apt to be involved; angina pectoris may be an early symptom;

¹ *Brit. Med. Jour.*, 1909, ii, 1509.

² *Jour. Path. and Bact.*, 1907, 12, 11.

³ *Am. Jour. Med. Sci.*, 1918, 155, 92.

aortic insufficiency is often associated with it; the aneurisms are frequently multiple, five, seven, and nine have been described; the small cup-formed sacs, of which there may be four or five in the ascending arch, are almost always syphilitic; other luetic features may be present, gummata of the liver or bones; there are signs of locomotor ataxia or the husband may have tabes and the wife aneurism, or both husband and wife have aneurism; in a large proportion of cases the Wassermann reaction is positive; and lastly, antisyphilitic remedies may relieve the symptoms.

Other acute infections play a less important rôle. There are two ways in which aneurism may be associated with the specific fevers. In any one of them local spots of degeneration, usually of the intima, may occur, or patches of mesaortitis may develop, leading to a weakening of the wall. Thayer and others have shown the frequency of these changes after *typhoid fever*, and the same may happen after *influenza*, *pneumonia*, *erysipelas*, and *scarlet fever*; there is doubt about *malaria*, upon which some of the French writers lay stress. The other way is associated with the *endocarditis* of the specific fevers. Direct extension to the aorta from vegetations on the valves may take place, but more frequently the process is embolic, with patches of mesaortitis over which the intima ruptures, just as occurs in the experimental production of aneurism. In the aortitis of *rheumatic fever* one or other of these forms may be followed by aneurism; but many of the cases described as aneurism of the aorta in this disease are instances of the dynamic dilatation associated with aortic insufficiency and a huge left ventricle. But true aneurism does occur. In a case reported by Renon, the patient, aged sixteen years, developed signs of aneurism very rapidly with aortic insufficiency in the course of rheumatic fever. Death occurred from hemorrhage. The type in the acute infections will be considered in a special section on mycotic and embolic aneurisms.

Tuberculosis is frequently met with as a complication of aneurism, 25 to 29 per cent. (Soltau Fenwick), but it plays a very minor part in the etiology, except of the erosion form occurring in tuberculous cavities in the lungs. The aorta or one of its main branches may be eroded from without by a tuberculous gland with the formation of an aneurism.

Intoxications.—*Alcohol* favors arterial degeneration perhaps directly, but more often indirectly. *Tobacco* which has been shown experimentally to have an important influence in causing arterial degeneration, has no part in the etiology of aneurism. *Lead* has, in man, a decided action in causing degeneration of the arteries and in this way predisposes to aneurism but the causes of arteriosclerosis and aneurism are by no means identical.

Embolism as a Cause of Aneurism.—In 1888 a man died in the Montreal General Hospital with fever and signs of aortic insufficiency and aneurism. The postmortem revealed an extraordinary condition—acute endocarditis of the aortic segments, with five aneurisms in the arch of the aorta. The largest of them, the size of a billiard ball, projecting to the right just above the aortic ring, was very thin-walled and had numerous greenish vegetations on its lining wall, which at one point

had perforated into the pericardium. The intima of the aorta was smooth. and on the arch above the larger aneurism were three small ones not larger than cherries. From the side of the intima they were not visible, but their site was indicated by the pressure of small, fungoid outgrowths. These were seen on the edges of narrowed slits of the intima which led directly into the small, saccular aneurism. This was the first instance in which the *mycotic* character of this type of aneurism was recognized. It has since been studied very carefully by numerous observers, most recently by Reifenstein.¹

There are two modes of formation: (a) In the smaller vessels the condition, as described by Ponfick and by Pel, is due to the direct lodgment of emboli with infection and erosion of the wall and the production of an aneurism. A number may occur in different vessels. Libman reports a case with four aneurisms on the mesenteric vessels, a fifth on the right branch of the hepatic artery, a large one on the right femoral, and before death, right hemiplegia with aphasia probably from rupture of a mycotic aneurism of the left sylvian artery. In another case of Libman's, with mitral and aortic endocarditis, a mycotic aneurism of the left femoral artery perforated the vein with the formation of an arteriovenous aneurism. In this form there is no question of the direct local infection of the intima by the emboli.

(b) In the case of the *multiple mycotic aneurisms* of the aorta, it is a different matter. Here, in all probability, the emboli pass to the vasa vasorum and cause a mesaortitis with weakening of the wall. The intima splits, and in this way a small aneurism is formed. In the case reported by the senior writer, and in other instances, particularly the one reported by John McCrae,² splits in the aorta were sharp and defined as if made with a knife. There may be no disease of the intima itself in the neighborhood. With this view Eppinger concurs, and he remarks that the multiplicity of the lesions within a small radius is evidence of the embolic nature. In other instances there is a verrucose aortitis which has extended directly from the valves and is not of an embolic nature; and in a few rare instances this occurs in rheumatic fever. Embolic aneurisms are not always mycotic. A fragment from a calcified vegetation dislodged into the circulation may lacerate the intima at the point of lodgment with the formation of a traumatic aneurism. The senior author saw a remarkable case of this kind in the Radcliffe Infirmary with Dr. Mallam: A man with aortic insufficiency and a remarkable musical diastolic murmur, had been under observation for a long time, and had frequently been used for examination purposes. Suddenly one day he had an agonizing pain in the calf of one leg, which became swollen, hot, and painful. As the swelling subsided a pulsation was noticed, and he recovered in a few weeks with a well-marked aneurism of the posterior tibial artery. The musical quality of the diastolic murmur disappeared entirely. No doubt a small calcified spike at the edge of one valve had been dislodged. A large majority of the cases occur in connection with ulcerative endocarditis. Pain of an agonizing character is present in the area where

¹ *Am. Jour. Med. Sci.*, 1924, **168**, 381.

² *Jour. Path. and Bact.*, 1905, **10**, 373.

the emboli lodges. Periarteritis, swelling, and infiltration of the surrounding tissues usually occur, and it may not be until their subsidence that the pulsation is noticed.

Relation of Aneurism to Atheroma.—Everyone who has made many postmortems, particularly in very old people, must have been struck with the fact that the extent of atheroma bears no relation whatever to the frequency of aneurism. The aorta may be a calcified tube, with an intima as rough as the skin of a crocodile, without the presence of aneurism. The truth is the *endarteritis deformans* of Virchow is not necessarily associated with weakness of the media and adventitia. Chiari made a careful comparison between a series of cases of ordinary atheroma of the aorta and of mesaortitis. Of his conclusion, which has special importance in the differentiation of these two groups, a summary may be quoted: "In atheroma he found a primary change in the intima, a thickening with a tendency to hyaline, mucoid, or fatty degenerations, leading to necrosis or calcification. In the early stages the media and adventitia appeared normal. In the later stages changes similar to those in the intima appeared in the inner layers of the media, while the outer layers showed proliferation of the vasa vasorum with small-celled infiltration around them, and in the adventitia there was in some cases considerable infiltration around the vasa vasorum, the walls of which showed some degree of proliferating endarteritis. These inflammatory changes, however, remained localized, and even in advanced cases did not reach a very great degree of intensity. Only by the actual pressure of a large calcareous patch was the media destroyed to any great extent. He considered that such a condition could be produced by any injury to the vessel, infections or intoxications, or the disturbance of nutrition which accompanies old age" (abstract by C. N. Aitchison, M.B.¹). In other groups the change was a mesaortitis in syphilitics or the subjects of general paralysis and the intima presented the furrows and scars already described.

High Blood-pressure.—Next to destruction of the elastic fibres of the media by a mesaortitis this is the most important single factor in the causation of aneurism. It acts in two ways: if permanent it leads to arteriosclerosis and weakening of the media, so that there is dilatation, either diffuse of the aortic arch or in spots. More important still is the sudden increase of tension following a rapid movement or severe strain. By an internal trauma over the weakened media the intima may tear with the formation of a small sac. The process may be traced in the production of *experimental* aneurism. With epinephrine, tobacco, and bacterial poisons, extensive degeneration of the aorta and larger vessels is caused, but what is most interesting in this connection is the formation of aneurisms, either (1) multiple bulgings in areas in which the media is greatly weakened, causing pouch-like aneurisms, just such as we see in the endarteritis deformans of old people; or (2) the normal-looking intima is split over an area of mesaortitis, a clean-cut, knife-like incision,

¹ *Deutsch. med. Wchnschr.*, 1903, 29, 5, 330.

beyond which is a little saccular dilatation or the beginning of a dissecting aneurism. These splits of the intima over local areas of degeneration, are identical with those met with in the human aorta.

External trauma has a definite influence on the causation of aneurism. Vesalius noted this in one of his cases. Many instances have followed blows on the chest, falls, or the jar of any accident. While rupture of the healthy aorta may occur in these cases it is more probable that the intima ruptures over a patch of mesaortitis, and in this way the aneurism starts. Stern¹ has collected a large number of cases from the literature. The aneurism may appear in a few days or not until many months have passed.

In a few rare cases aneurism of the aorta is of the *erosion* type. A tuberculous focus may involve the wall of the aorta, as in a case reported by Councilman. A bullet lodged in the wall without perforating it has been followed by aneurismal dilatation (Freyham).

Mickle called attention to the frequency of aneurism in the *insane*. This and the coexistence with *locomotor ataxia* is a syphilitic association. Lee Dickenson² described aneurism in connection with *hypoplasia of the aorta*. Both of his cases were in young adults with thin, narrow aortas, free from disease; one presented three aneurisms. Richey³ reported the case of a boy, aged sixteen years, who died suddenly from an intra-pericardial rupture of an aortic aneurism, associated with hypoplasia of the aorta and status thymico-lymphaticus. Goehring⁴ described a case of congenital aneurism of the aortic sinus of Valsalva and collected 6 others from the literature.

Number, Form, and Size of Aneurism and Vessels Affected.—*Number.*—In the aorta the aneurism is usually single, but three, four, five, even a score or more, may be present. The multiple cup-shaped tumors in young men are always syphilitic. The mycotic aneurisms are often multiple; in one of the senior writer's cases there were five in the arch of the aorta. In the embolic form there may be a dozen or more in the smaller vessels. In certain individuals aneurism may occur in different vessels, simultaneously or in succession.

Form.—In the aorta there are two great types, the *cylindrical*, or *fusiform*, and the *sacculated*. In his study⁵ Thoma calls attention to the physiological bulgings of the aorta: "The ascending aorta in the region of the semilunar valves presents an onion-shaped dilatation, the *bulbus aortæ*, in which are the sinuses of Valsalva. Immediately above the valves the lumen narrows distinctly, becomes circular, and then undergoes a second dilatation directed forward and to the right, known as the *sinus quartus sive maximus Valsalvæ*. This unilateral, spindle-shaped dilatation of the aorta also disappears again before the vessels of the neck are given off. After the origin of the left subclavian there follows a narrower portion of the lumen, the *isthmus aortæ*, after which the vessel again widens." As given in the plates illustrating the article,

¹ *Ueber traumatische Entstehung Inneren krankheiten l. c.*, 1896, 70–74 (G. Fischer, Jena.).

² *Trans. Path. Soc.*, London, 1894, **45**, 52.

³ *Arch. Int. Med.*, 1923, **31**, 232.

⁴ *Jour. Med. Res.*, 1920, **42**, 49.

⁵ *Untersuchungen über Aneurismen, Virchow's Archiv.*, 1888, **111**, 76.

Thoma shows that in pathological states of the arch these physiological bulgings are followed; one or other or all of them may show dilatation, or the whole arch may be involved, forming a definite spindle. In other instances the arch is a huge, flabby sac scarcely retaining a semblance of its shape. Typical spindles are seen too in the arteries of the second and third dimensions, rarely in the smaller vessels. The cylindrical and fusiform are usually combined, as the dilatation tapers at either end. Sometimes the whole aorta or a large section of it is represented by an enlarged cylinder.

The *sacculated* form, in which there is a definite protrusion of one side of the wall, is the more common. The shape of the sac will depend on the extent of the area of the primary weakness of the wall; if large, the sac will be diffuse and crater-like; if small in relation to the aorta, it may have a small orifice, slit-like, oval, or round, leading into a circular pouch. Some sacs are flat, saucer-shaped, others cup-shaped, others pear-shaped, almost pedunculated, with a narrow neck. The saccular aneurism may arise on the wall of a diffuse dilatation, or a saucer-shaped sac may have two or three small ones upon it. Occasionally there is seen an aneurism of multilocular aspect, which has arisen from the excessive development of these secondary sacs.

In the small arteries, as of the brain and kidneys, these same types are seen—the saccular more often than the fusiform. The special forms of dissecting and arterio-venous aneurisms will be described later.

Size.—From a pin's head to the head of a child. There are almost microscopic tumors of the small arteries, while a sac connected with the aorta may fill one-half of the chest. When perforation of the chest wall occurs, or when there is a diffuse aneurism of the abdominal aorta, the size of an adult head may be reached, and with its contents the aneurism may weigh 5 or 6 pounds.

Life History of an Aneurism.—Against the incessant strain offered by the pumping of blood sixty to eighty times a minute, the artery is protected by the elastic and fibrous tissues of the media and adventitia. Weakened at one spot and yielding, it is then a struggle between the blood-pressure and the remnants of the tube at the affected spot—an unequal struggle, as the sac gradually yields. But Nature does not rest passive. Only in the very acute cases is no attempt seen to limit the mechanical progress of the disease. In nearly all aneurisms healing is attempted by two processes, with two tissues, the one mural and the other hemic, a new growth of connective tissue and fibrin formation.

(a) Connective-tissue healing of an aneurism, seen to perfection only in small forms, is an intimal affair; in large sacs the adventitia plays the chief part. We owe to Thoma the first good account of this method of healing. Fig. 95, here reproduced, shows a small sac on a branch of the ophthalmic artery entirely obliterated, with a growth from the intima in such a way that the inner surface of the artery and of the sac are on a level. Although the same process may go on in the large vessels (and Thoma figures an example in the abdominal aorta), it is much less rare than in the small branches. In every aneurism still lined with intima this compensatory thickening is to be found. But

under the influence of the blood-pressure the sac, as a rule, grows at such a rate that the endarteritis cannot keep pace with it. In the common saccular aneurism the reparative process from the adventitia is much more important. There is active proliferation of the fibrous elements, and although it may yield and be thin at the point of greatest pressure, in the larger sacs there is found great thickening which is not always easy to differentiate from the surrounding connective tissue.

The *lining* of an aneurism may be the thickened intima (which is only the case in very small tumors), the media, in whole or in part, or, as the sac enlarges, the adventitia alone. Then comes a stage in the growth of the larger tumors in which part of the sac is no longer composed of an arterial coat, but is in direct connection with adjacent tissue, bone,

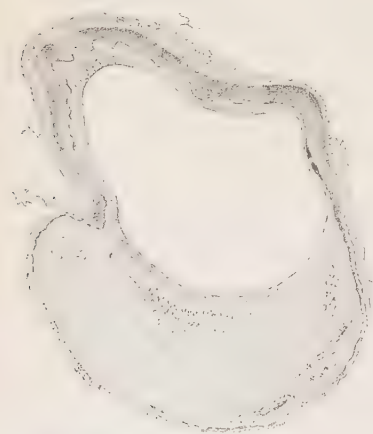
lung, skin, or the structure of the mediastinum. In the big dilatation aneurism the intima may be everywhere unbroken, but thickened and roughened with calcareous plates and areas of atheromatous softening. In the saccular form the intima may be traced only to the orifice or for a short distance into the wall of the sac.

(b) The second great element in the repair of an aneurism is *thrombosis*, the deposit of laminated fibrin in the sac. It does not occur in every case, even under conditions which look the most favorable. In a typical degree the deposition of fibrin is seen in the sacs with narrow necks, but it may be seen in the fusiform dilatation of any part of the aorta. In cutting across an aneurism in which this process has been going on,

firm, hard, leathery sheetings of grayish-brown fibrin are seen, arranged in layers which may be peeled off like the flakes of an onion. In large sacs from 25 to 50 laminæ may be counted. The gradual formation of these is most interesting. One often finds on the lining membrane of a small-sized sac most remarkable deposits of platelets, usually ribbed like sand on the seashore or arranged in a tracery or network. The areas with the platelets show as grayish-white, soft thrombi, quite different in appearance to the reddish-brown ground substance on which they are deposited. Gradually the aneurism may become filled even to the mouth, and in this way permanent healing may be effected. At first the layers of fibrin are reddish-brown in color, but in the very old sacs they are grayish-white, and occasionally lime salts are deposited, so that the whole becomes a firm, calcareous mass.

Pressure Effects.—With the gradual growth of the sac remarkable effects of compression are seen. Passing anteriorly, an aneurism of

FIG. 95



Cross-section of the ophthalmic artery showing diffuse arteriosclerosis and healing of an aneurism by intimal thickening. (After Thoma.)

the arch erodes the sternum, destroys the costal cartilages, fractures the ribs, which gradually become absorbed, and finally, there may be a hole in the front of the chest into which the two fists may be placed. Posteriorly, an aneurism of the descending thoracic aorta may perforate the chest wall and destroy four or five ribs, causing complete atrophy of the muscles in its course, and appear beneath the skin as a large flabby sac, as is very well shown in Fig. 100. Not less remarkable effects of erosion are seen in the spine, the bodies of three, four, or five of which may in large part be absorbed and the roughened bone forms part of the wall of the aneurism. A remarkable fact, noted by Morgagni, is that the intervertebral disks are not destroyed at the same rate as the bone, and may remain more or less intact while the bodies are deeply eroded. The exact method of this destruction of bone is much discussed. Some have ascribed it to a dissolving action of the blood, others believe it to be entirely mechanical, due to the pressure and shock of the systole. Cornil and Ranvier describe it as a rarefying osteitis, a low grade of inflammation by which the bone is gradually removed. Other effects of compression and the modes of perforation will be described later.

ANEURISM OF THE HEART

1. Aneurism of the Valves.—Weakness of the tissue of the valve results from erosion, from mycotic ulceration, or from softening of an atheromatous focus. There are acute and chronic forms. The acute valvular aneurism is seen most commonly on one of the aortic segments projecting from the ventricular side in globular form of the size of a pea or of a small nut. Sometimes it involves the entire valve. It may be at the line of attachment, so that there is partial aneurism of the sinus of Valsalva as well. It may be the only lesion, although more frequently it is associated with destructive changes. In very many instances the aneurism is perforated. Two, three, or even four little sacs have been found. Involvement of the mitral segments is not so common—the anterior valve more frequently than the posterior. The chronic atheromatous aneurism is a very different affair. Following the softening of a subintimal focus, it is usually seen in sclerotic or partially calcified valves, and in the aortic more often than in the mitral segments. Thrombi may be deposited; in one instance they were firm and laminated.

2. Mural Aneurism.—Two forms may be recognized, the acute and the chronic.

Acute Aneurism.—Acute aneurism, an event in connection with ulcerative endocarditis of the heart wall, is seen most frequently on the left side in the upper portion of the septum near the aortic ring, but it may occur on the right ventricle, and even in the auricles. Perforation is apt to take place into the pericardium or one of the other cavities, or into one of the larger vessels. A variety of this is the dissecting aneurism of the heart, of which Vestberg¹ has collected 60 cases.

Chronic Aneurism.—This is an event in connection with fibrous myocarditis. It is not very uncommon, particularly the slighter forms.

¹ *Nordiskt Med. Arkiv.*, 1897, 7, Nos. 26 and 31, 1; 1.

Strauch¹ collected 55 cases which occurred in Berlin, chiefly at the Charité Hospital within ten years. There were 3 cases at the Johns Hopkins Hospital among 3000 postmortems. It is much more common in men than in women—64 out of 80 cases (Wickham Legg²); 38 out of 55 cases (Strauch). The majority of the patients are above fifty years of age. A case has been reported in a boy of ten (Rosenstein).

Etiology.—The etiological factors are those of arteriosclerosis and chronic myocarditis. In Strauch's series 44 of the cases presented myocarditis alone without valve lesion. It is usually stated and it certainly was the senior writer's experience, that the coronary arteries are involved or the anterior branch is calcified and narrowed; but Strauch's cases do not bear out this view, as only 15 showed involvement of the coronary arteries. He regards it as a special pathological change, a degeneration which is difficult to connect with any other heart lesion. Syphilis did not appear to be a factor in many cases. The left ventricle is affected in almost every instance, in all of Strauch's series, and in a large majority the apex region is involved, extending toward the septum. Usually single, there have been cases reported with two or even three aneurisms. In the most characteristic form there is a globular distention of the apex region of the heart, with perhaps slight thickening of the pericardium or a definite change in the appearance of the muscle. The tumor may be the size of the fist, or even larger. From within thrombi are usually seen, attached to a sclerotic endocardium. On section of the wall of the sac the heart muscle may in great part be converted into fibrous tissue. The thrombi have been found calcified. As a rule, the sac is flat, in a few cases quite globular and communicating with the cavity of the ventricle by a narrow orifice. Cases have been described in which the sac has been larger than the heart itself.

Symptoms.—The symptoms are very obscure, and it is rarely possible to make a diagnosis. The cases are usually mistaken for chronic myocarditis, or the diagnosis is made of the associated valvular lesion. As the aneurism is at the apex and enlarges the left ventricle, the features of hypertrophy and dilatation are usually present. Symptoms of angina pectoris are not infrequent. Strauch analyzed the signs in a select group of cases without throwing any special light on the diagnosis.

DILATATION ANEURISMS

There are two important groups: (1) In one, seen chiefly in the aorta and larger branches, the artery has passively dilated, owing to disease of its walls; (2) in the other, seen most frequently in small branches, there is an active dilatation due to growth and enlargement of the vessel.

Dilatation Aneurism of the Aorta (Dilatation of the Aorta: Chronic Aortitis).—New interest has been attached to this form since the introduction of the roentgen-rays in clinical diagnosis. Formerly it was overlooked to a great extent even in the best clinics as proved by the striking fact that of the long series of cases studied by Thoma³ scarcely one had

¹ *Ztschr. f. klin. Med.*, 1900, **41**, 231.

² *Med. Times and Gaz.*, London, 1883, **2**, 199.

³ *Virchow's Archiv.*, 1888, **111**, 76.

been recognized in the wards, though under the care of one of the most skilful clinicians in Europe.

Joseph Hodgson,¹ in 1815, described what he called "a preternatural, permanent enlargement of the cavity of an artery," and distinguished it clearly from ordinary aneurism. He recognized its association with disease of the coats of the vessel, and remarked that saccular aneurism could be engrafted upon it. The dilatation, which might be partial or complete, affected most frequently the ascending aorta. He very acutely observes that the symptoms suggest organic disease of the heart rather than aneurism. Since Hodgson's date this form has been well recognized anatomically, but it has not received enough consideration clinically. Scarpa, while recognizing dilatation of the whole tube of the aorta, regarded it as essentially different from aneurism, although he says the two may be sometimes found together. Morgagni made a clear division between two kinds, one in which the tumor occupies the whole circumference of the arterial tube, the other in which the aneurism only affects one side of the artery. Primarily a disease of the media causing weakening, there are usually associated changes in the adventitia and extensive alterations in the intima. Among the forms recognized by Thoma are: (1) the multiple spindle-shaped aneurism; (2) the single fusiform aneurism; (3) the saccular engrafted or spindle form; and (4) the tent-shaped or sphenoid, a special form in connection with the upper part of the thoracic aorta, which he thinks, results from abnormal tension at this point just where the upper intercostal arteries are given off. He lays great stress on the involvement of the adventitia, and with the periarteritis he would associate the attacks of pain so common in this condition. While, as a rule, this form is met with in old persons and is associated with extensive endarteritis deformans, one meets with a few cases in which the arch is considerably dilatated with a smooth or not much involved intima.

Associated quite frequently with this dilatation of the arch is insufficiency of the aortic valves, due either to a sclerosis and shortening of the segments or to dilatation of the ring itself. It is to this combination particularly that the French give the name, *Maladie de Hodgson*, but in the original description of this author it does not seem that he refers to the associated disease of the valve.

In young men with syphilis the process may be limited to the arch, which in any case is most common, but it may involve the entire aorta. In nearly all cases there is extensive endarteritis deformans with calcified laminæ and atheromatous erosions. The dilatations may be onion-shaped or spindle-formed. They may be multiple. Sometimes on the wall of the spindle-formed dilatation there are small saccular aneurisms. Thoma's admirable paper gives outline figures of the various forms, all of which owe their origin directly to the action of blood pressure on the diseased vessel wall.

The dilatation aneurism is very common, particularly in old people, and is often found accidentally. Only when of a very large size does

¹ *A Treatise on the Diseases of Arteries and Veins*, London, 1815, p. 45.

thrombus formation take place in it. There is a remarkable specimen in the McGill Museum presented by R. L. Macdonell, in which the descending thoracic and abdominal aorta, and the iliacs were greatly dilated. The abdominal aorta forms a fusiform aneurism, which is filled with a densely laminated thrombus. In other instances the whole aorta is dilated, or the arch may be double or treble the normal size and without thrombi on the roughened intima.

Etiologically, according to McCrae,¹ there are probably two main groups, one in which the dilatation occurs with an acute infectious disease, notably rheumatic fever and the second in which the factors are essentially those which cause arteriosclerosis and aneurisms.

Symptoms.—There are three groups of cases: (a) Latent: The condition is met with accidentally in medico-legal work or in the postmortem-rooms of almshouses and infirmaries, particularly among old people. The dilatation may reach an extreme grade without any special symptoms. (b) With the picture of *angina pectoris*: In the syphilitic aortitis in men under forty years there may be no dilatation of the arch, but in the senile dilatation of the arch angina is a common, sometimes the only, symptom. The attacks of pain may recur at intervals for several years without any sign of cardiac insufficiency. (c) In a third group the features are those of organic disease of the heart, usually of aortic insufficiency, which may be present for weeks or months before the end comes. Hodgson recognized the fact that the clinical features of the condition were very often those of valvular disease. The incompetency of the valves may be due to the distention of the aortic ring.

Physical Signs.—*Inspection* may show a diffuse impulse over the manubrium, but in old persons with rigid chest walls and a calcified aorta there may be an extreme degree of dilatation without a visible impulse. The top of the aorta may reach to the sternal notch, and the innominate artery is elevated; but it is to be remembered that the throbbing in this situation is much more frequently due to the right carotid as it leaves the innominate, or to the innominate itself, than to the arch. The right subclavian is often visible above the clavicle. An impulse may be seen on either side of the sternum in the first and second interspaces. Palpation may detect a systolic thrill, rough and harsh in cases of calcification of the intima, sometimes diastolic when the valves are insufficient. With one hand on the manubrium, the other on the spine, pressure may detect a deep pulsation. In the sternal notch the forcible throbbing of the dilated aorta may be felt. Tracheal tugging may be present. *Percussion* gives dulness over the manubrium and sometimes in the adjoining first and second interspaces, varying with the extent of the dilatation.

Auscultation.—A systolic murmur may be heard and propagated into the vessels of the neck. There is nothing distinctive in it, nor does it differ from the bruit so often heard over the aorta in old persons with sclerosis. A diastolic murmur, if present, is more important, as it may be heard up the sternum, often quite loudly, and is even propagated into

¹ *Am. Jour. Med. Sci.*, 1910, **140**, 469.

the vessels of the neck. The aortic second sound may be of a remarkably metallic quality and loudly heard up the sternum. The fluoroscope shows a pulsating shadow, larger and higher in position than the normal aorta, and which does not disappear in diastole.

Active Dilatation Aneurism. Cirroid Aneurism.—No structures retain their powers of growth in greater degree than the arteries. Many physiological conditions demand the retention of this property; for example, the arteries of the uterus at term are four or five times as large as in the unimpregnated state. In tumors, in the enlarged spleen, in the proximal branches after ligation of a main trunk, the arteries not only increase in size, but there is an active development showing to what an extraordinary degree these structures possess the capacity for new growth. With this power it is not surprising that we meet with instances in which spontaneously, at any rate from unknown causes, arteries enlarge. The condition is known as aneurism by anastomosis, racemose aneurism, or, more commonly, *cirroid aneurism*. The arteries of the fourth and fifth dimensions are the most frequently involved vessels, for example, of the size of the radial and its immediate branches, or of the temporal arteries. The dilatation may be confined almost entirely to the arteries themselves. In other instances the veins are involved, and the smaller vessels, even the capillaries, may be implicated, so that the structures form a diffuse angioma. The situations most frequently involved are the head and the hands, but the arteries of any part of the body may be affected and the aneurism may be single or multiple.

There are three important exciting causes. The dilatation may arise in small birthmarks or little angiomas, particularly those about the ear and forehead. With a gradual increase in size, the arteries become convoluted and throb forcibly. In a second group of cases the aneurism follows directly upon an injury. And thirdly, in an interesting series of cases the tumor arises as a sequence or during an attack of fever. Two such cases are reported by Bazy.¹ At the Johns Hopkins Hospital we had a patient in whom multiple cirroid aneurisms were present: following an attack of typhoid fever there was a decided increase in the size of the vessels. Reverdin suggests that all sorts of infectious arteritis may be the starting point of the aneurismal dilatation.

Symptoms.—Small tumors may cause no inconvenience. There may be slight swelling of the skin over the bunch of dilated arteries, and when the hand is placed upon it the individual vessels are felt to be convoluted and dilated; the pulsation is forcible, there is usually a thrill to be felt, and with a stethoscope a loud whirring murmur is heard. If the arteries alone are dilated, this may be systolic and single. In other cases where there are large venous anastomoses, the murmur is more or less continuous with systolic intensification. In other cases, particularly about the ears and temporal region, the skin itself is involved. There is marked swelling with a bluish tint, the dilated arteries are visible, telangiectases are present in the skin, or, if the whole process has started

¹ *Gaz. des Hôpitaux*, 1889, 62, 1363.

from a small birthmark or a nævus, the entire tumor may present the character of an angioma. The side of the face and head may be involved, and exophthalmos be present on the affected side. Huge tumors of this kind are reported, and they have at times increased with the rapidity of a new growth. Arising spontaneously, they have been known to disappear in the same way. A remarkable case is reported by Ferrell.¹ A man aged twenty years, had a large pulsating tumor above the right clavicle which had lasted many years and which involved all the branches of the thyroid axis except the inferior thyroid; the transversalis coli and suprascapular could easily be made out, greatly enlarged and tortuous. During an attack of measles, in which the temperature rose to 106.5°, the tumor looked very red and angry, and pulsated very strongly, as if about to rupture. Following the attack of measles the tumor began to subside, gradually the pulsation and thrill disappeared, and it shrank to a mass of hard connective tissue.

DISSECTING ANEURISM

Splits and Fissures of Intima. Rupture of Aorta. Healed Dissecting Aneurism.—1. **Splits and Fissures of the Intima with Healing.**—In the artificial production of aneurism, there is sometimes found over a patch of mesarteritis a small slit or fissure of the intima, cleanly cut as if with a knife, evidently due to rupture. Behind this there may be a small pouch-like distention of the media and adventitia, or a little dissecting aneurism. Precisely the same thing happens in man, and there may be spontaneous rupture of the intima in the form of a small slit one-fourth to one-half inch in length, or the entire circumference of the intima of the aorta may be cut through as if with a knife. A most remarkable circumstance is that these lesions may heal completely, leaving scars of the most extraordinary character. The cases are not very numerous in the literature. Von Recklinghausen described the case of a woman who died postpartum of a rupture two inches long of the inner coat of the ascending aorta. In the descending aorta an inch below the duct there was a split of the intima completely encircling the tube which was entirely healed. Zahn reports a case of a woman, aged thirty-seven years, dead of pneumonia and an aneurism of the aorta. Sixty millimeters from the ring there were healed splits in the intima and the media. The latter coat was not quite cut through, and this he thinks was the cause why a descending aneurism was not formed.

By far the most important study in the healing of those splits and tears is in the well-known paper by Rokitsansky.² He had not at that time seen a case of complete healing of a dissecting aortic aneurism, but he well remarks that the healing of the tears of the inner coat of the aorta, which he had figured, are not less remarkable. He reports five cases of healed splits of the intima. In Deland's case, the heart of which was dissected by the senior writer, in the first attack the intima

¹ *St. Louis Courier of Medicine*, 1887, 17, 127.

² *Denkschriften der kaiserlichen Akademie der Wissenschaften, Wien.*, 1852, 4, 1.

of the aorta had split in the entire circumference and there was a fibrous cicatricial ring just above the valves. There was no pouching, and the margins of the intima were rounded and smooth. It looked an old and healed lesion. Farther up the arch was the fresh knife-like split of the intima and rupture into the pericardium.

FIG. 96



Illustrating a complete transverse split of the intima of the aorta. (After v. Schrötter.)

2. **Spontaneous Rupture of the Aorta.**—Traumatic rupture is not uncommon in medico-legal work. Spontaneous rupture is rare, but it may occur in a vessel apparently healthy, either as a result of sudden strain or sometimes without any effort. It may occur during confinement or in sudden muscular effort. It has occurred in a healthy boy aged thirteen following prolonged exertion. In the majority of the cases it is an intrapericardial rupture. The intima may be smooth and the lesion is usually sharp and well defined, as if cut with a knife. The rupture in the external coat is rarely directly opposite that in the intima, so that there is usually some evidence of dissecting aneurism. The cases present very characteristic clinical features, the symptoms occurring in two stages.

The case reported by Lynn¹ is a good illustration: a woman, aged twenty-nine years (who had twice miscarried), in her third pregnancy, within fourteen days of term and without any special effort, complained of pain in the side and cardiac oppression. During labor, just after a pain, she started up in bed with an agonizing pain in her heart, and said she was dying. She became cold and pale and pulseless. She revived for a few minutes and was delivered in about two hours of a dead child. She remained cold and faint, with a small, quick pulse, and Lynn thought the heart was ruptured. She improved gradually and seemed to be doing very well until the fourteenth day after delivery, when she again

¹ *Medical Records and Researches*, London, 1798.

complained of a sudden pain in the chest, and she died in a few minutes. A very good illustration accompanying the paper shows an aortitis with rupture into the pericardium. In a woman at this time of life, who had had miscarriages and such a condition of the aorta, the trouble was no doubt due to syphilis. Of the two clinical periods, one corresponds to the rupture of the intima, with which is associated the severe pain and collapse, from which the patient gradually recovers. Then in the course of three or four days external rupture takes place with sudden death. In some instances the interval may be for fourteen days.

3. **Dissecting Aneurism.**—In ordinary practice and in the work of a general hospital, dissecting aneurism is not very common. There were only 2 cases in sixteen years at the Johns Hopkins Hospital, where aneurism may be said to be exceptionally frequent. And yet it is a common event, particularly in medico-legal work. A most interesting collection is in Boston, where, in the Warren Pathological Museum, there are 20 cases of dissecting aneurism and rupture of the aorta, most of them collected by the late J. B. S. Jackson. The senior writer is indebted to Joseph Pratt for getting the details about the cases. Apart from the traumatic instances, there are two groups of cases: the first, occurring in comparatively young persons, results from a rupture of the intima over the middle and external coats, weakened by syphilitic or some other form of aortitis. In the second group, occurring in elderly or very old people, there is extensive endarteritis deformans, and the rupture takes place at the edge of an atheromatous erosion, or an atheromatous intima may be split during a sudden exertion. The most frequent site is the arch and in its ascending portion. But the rupture may occur in any part of the aorta or in one of its main branches.

In regard to the *pathogenesis* there are three theories: (a) Traumatic, *i. e.*, a violent muscular effort or other factor which would cause a sudden marked rise in the blood-pressure: (b) a chronic high blood-pressure such as that due to hypertrophy of the left ventricle with competent valves: (c) disease of the vessel wall either of the intima or media or both. Babes and Mironescu¹ believe that dissecting aneurisms are due for the most part to a primary disease of the media which they termed “mesarteritis dessicans” and which may occur independently. This view receives the support of Moriani,² Krukenberg,³ and Whitman and Stein.⁴

One of the early cases in which it was recognized was that of George II, who died suddenly of a rupture of the right ventricle. There was in addition in the trunk of the aorta a transverse fissure an inch and a half in length, through which blood had recently passed under its external coat and formed an elevated ecchymosis. As a rule, the blood infiltrates between the layers of the media, sometimes between the media and the adventitia. The extent of the splitting varies from a small area, such as that reported by Nicholls in the case of George II, to a complete separation of the coats of the entire aorta. There are instances on record in which the blood has passed down the crural arteries far into the vessels of the legs. Rupture may take place externally, which is

¹ Ziegler's Beitr., 1910, **48**, 221.

² Ziegler's Beitr., 1920, **67**, 329.

³ Virchow's Archiv., 1910, **202**, 283.

⁴ Jour. Med. Res., 1924, **44**, 579.

very frequent, into the pericardium, for example, or internally in one or more places into the lumen of the aorta itself. The extent of the circumference of the vessel involved varies very greatly. In some instances only a small section is involved, in others there is a separation of a large part of the circumference, and the vessels may be torn across, although more frequently they are spared. In some cases the intercostal arteries, the cœliac axis, the renal vessels, and superior mesenteric have been torn across. A great majority of the cases of dissecting aneurism prove fatal. The symptoms are those already mentioned in connection with spontaneous rupture of the aorta, a sudden sharp pain, collapse, and death follows in from two to fourteen days from bursting of the aneurism. A detailed description of the clinical history and course of dissecting aneurism was given by Peacock¹ and more recently by Moosberger,² Resnick and Keefer.³ The latter calls attention to the occasional development (4 times in about 300 cases in the literature) of signs of aortic insufficiency in cases in which the postmortem revealed normal aortic valves. Further in the majority of cases the heart is conspicuously enlarged, another point of analogy to an arteriovenous aneurism. But in a few cases recovery takes place with an illustration of the most remarkable reparative processes seen in the human body, the formation of a healed dissecting aneurism.

4. **Healed Aneurism.**—Shekelton,⁴ a Dublin surgeon, first reported cases of this kind, one of the abdominal aorta and the other of the left common iliac. In his first case so similar was the structure to that of the artery that he was inclined to regard it as an anatomical anomaly, but in the second case the doubt was cleared. Henderson,⁵ of Edinburgh, in 1843, reported a remarkable case, in which from just behind the origin of the left subclavian the entire aorta consisted of two tubes. The outer canal communicated with the inner through an orifice into the left common iliac artery. The outer tube did not extend around the entire circumference. Both Shekelton and Henderson appreciated the true character of this remarkable condition. But Hope, in his well-known work on *Diseases of the Heart*, in referring to a case, thought that it was a congenital anomaly, a double aorta. Indeed, when one sees a specimen it is not surprising that this mistake has been made. The best accounts of the condition are given by Boström,⁶ and by Adami,⁷ who collected altogether 39 cases, among which women were almost as numerous as men. In a majority of the cases there was no advanced disease of the aorta. This is as we should expect, since it is due to weakening of the media, and the intima may show little or no atheroma. The site of the primary rupture was in the ascending aorta in 13 cases, below the origin of the left subclavian in 12 cases, the lower part of the thoracic aorta in 5 cases, in the abdominal aorta and iliac artery 1 case each. The

¹ *Trans. Path. Soc.*, London, 1863, **14**, 87.

² *Schweiz. Med. Wchnschr.*, 1924, **54**, 325.

³ *Jour. Am. Med. Assn.*, 1925, **85**, 422.

⁴ *Dublin Hospital Reports and Communications*, 1822, **3**, 231.

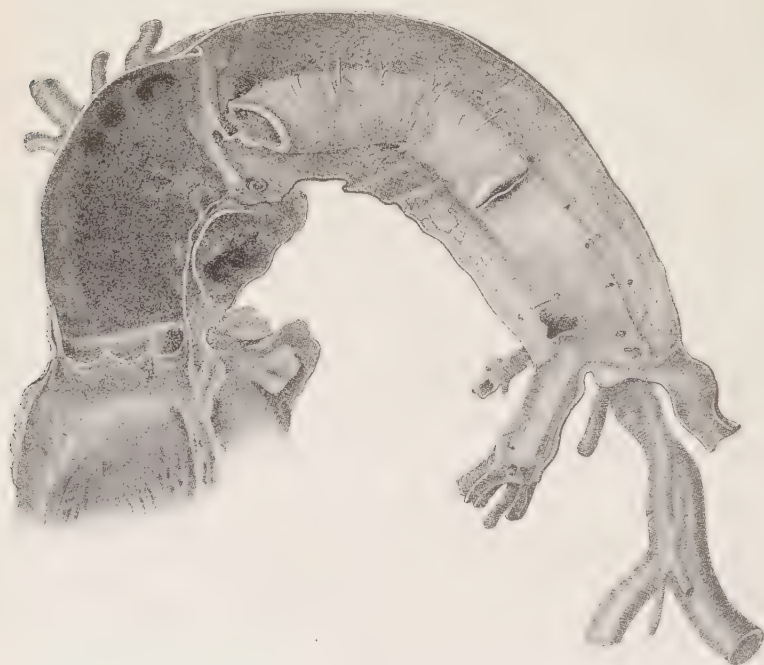
⁵ *London and Edinburgh Monthly Jour. of Med. Sci.*, 1843, **3**, 613.

⁶ *Deutsches Archiv. f. klin. Med.*, 1888, **42**, 1.

⁷ *Montreal Med. Jour.*, 1896, **24**, 945.

outer tube may extend the entire length of the aorta and occupy a variable section of the circumference. The branches of the aorta very frequently take origin from the outer sac. A feature which perhaps attracts most attention and has no doubt led to the belief that in these cases a congenital anomaly exists, is the smooth, natural appearance of the outer tube. Rindfleisch showed that a growth of endothelium took place, with the formation, in part at least, of a new intima.

FIG. 97



Healed dissecting aneurism. (After Boström.)

The duration extends over many years. When a student in Toronto, the senior writer frequently visited the gaol with his teacher, Professor Richardson, and at intervals they saw there a soldier who had been discharged from the British army soon after the Crimean War for aneurism. He seemed a very healthy man, and there was no evidence of any existing tumor. He died in 1886, and J. E. Graham reported the case. There was a small healed aneurism at the third portion of the arch, and from the margin of this sac, just beyond the left subclavian, the aorta formed a double tube. There was little question that this had lasted for more than thirty years from the time of his discharge from the army with aneurism.

SACCULATED ANEURISM

As the great majority of cases of sacculated aneurism in medical practice affect the aorta, we shall deal with the disease as it is met with

in this vessel. For convenience of description we may divide the aorta into three parts—the arch, the descending and the abdominal portions:

Aneurism of the Arch of the Aorta.—As already mentioned, this part of the vessel may be uniformly dilated, but it is much more common to have one or other portion involved in a saccular aneurism situated in a sinus of Valsalva, the ascending or the transverse portion of the arch.

FIG. 98



Aneurism of the thoracic aorta.

FIG. 99



Aneurism of the subclavian artery.

Aneurism of a Sinus of Valsalva.—Aneurism of a sinus of Valsalva is a common and important variety, met with particularly in syphilitic subjects and in comparatively young men. There may be a pouching of all three sinuses, but more commonly one only is involved. The orifice of a coronary artery may be given off from the sac, and the first part of the vessel may itself be dilated. The aortic ring may become involved and the adjacent semilunar valve may be rendered incompetent. The aneurism may perforate one or other auricle from the right posterior sinus, or into the pulmonary artery or the right ventricle from the left posterior sinus, or from the anterior; or the sac may pass beneath the ring and perforate into the left ventricle itself. By far the most common perforation is into the pericardium; or rupture may take place into the superior vena cava. There are cases in which the aneurism seems to be given off directly at the aortic ring and involve as much of the ventricle as of the sinus.

Aneurism of this portion of the arch has very definite features: (a) It is not detected in the wards, but is seen in the dead-house, particularly in connection with medico-legal work. (b) It is very often latent, death occurring from perforation before there have been any symptoms. (c) It is frequently syphilitic. (d) Angina pectoris may be an early feature. (e) Aortic insufficiency is a common accompaniment.

Aneurism of the Ascending Arch.—Perhaps the most common situation for the sacular tumor is from the convexity of the aorta, an inch or so above the valve. The tumor grows freely to the right, displacing the vena cava and the lung, and some of the largest sacs met with originate in this situation. Anteriorly, it appears to the right of the sternum, in the second and third interspaces, and may gradually erode the bone and cartilage, and, passing upward, lifts the sterno-clavicular joint and appears as a large, external tumor. The sac may perforate into the pericardium, the right auricle, the superior vena cava, the lung, the right bronchus, or passing backward, erode the spine.

Aneurism of the Transverse Arch.—Owing to the very small space between the spine and the sternum, the tumor here is restricted in its growth, and is likely to cause early and severe symptoms from pressure, particularly upon the windpipe. The left recurrent laryngeal is involved, and changes in the voice, attacks of dyspnoea, and painful dysphagia are common. Small tumors may cause the most intense symptoms without, indeed, any physical signs. Although in this situation the sac, as a rule, does not grow to such a size, yet there are instances in which the extension laterally has been enormous, producing some of the largest and most chronic types of aneurism. Growth backward may involve the spine, producing agonizing pain.

Physical Signs.—*Inspection.*—The well-known dictum may be taken as a text: "More mistakes are made by not looking than not knowing." A majority of aneurisms of the thoracic aorta present suggestive features to the eye, but the inspection must be made with care. A good light, good eyes, a bare chest, and system are indispensable. Even in a good light one may look directly at a pulsation and not see it. The point of view is everything, and it is best to examine the patient on a revolving stool, which can be turned easily so as to get the effect of the light falling at different angles. Good eyes are the physician's best tools, but it is not merely acuteness of vision, though this is important, but it is the educated, seeing eye, which is only to be had by careful training.

"Strip to the buff" is the rule. If the shirt and undershirt are tucked up to save time, the all-important area above the level of the second rib may be covered. More than once it has happened in the senior writer's experience to have the sought-for diagnosis stare at the astonished doctor from the first or second interspace or the supraclavicular region. System is most important. Turn the patient and examine the back, particularly the interscapular areas. If not done in order as a routine, the chances are that it will be forgotten as the interest increases in other parts of the examination, and perhaps the diagnosis may be missed altogether. Certain cases make an enduring impression on one. In 1888 the senior writer saw, at the Girard House in Philadelphia, a man with orthopnoea, a greatly

dilated heart with an unusual widespread impulse in the lower sternum and adjacent parts. There was a loud, diastolic murmur, and the whole trouble had been attributed to aortic insufficiency. But there were very puzzling features in the case, which need not here be discussed. After finishing the examination in front the patient's back was turned to the light, when the diagnosis was instantly seen in the form of a prominent pulsating tumor in the left interscapular region, which had been overlooked. The senior writer on several occasions has missed the diagnosis by carelessness in the routine examination. In a patient named McKinley, very well known to a succession of classes at the Johns Hopkins Hospital, when first seen at the out-patient class, we were so interested in the physical signs in the front of the chest, which were those of a very obscure heart trouble, that we forgot to look at his back. In the ward the House Physician made the diagnosis for us on inspection of the patient's back. There is no disease more conducive to clinical humility than aneurism of the aorta. Mistakes occur with the most careful and the most skilful. Sometimes the diagnosis is beyond our art; more often it is not made because of the carelessness that so easily besets us in our work. The confession of the great Pirogoff always seems to me most touching: "There are in everyone's practice moments in which his vision is holden, so that even an experienced man cannot see what is nevertheless perfectly clear, at least I have noticed this in my own case. An overweening self-confidence and preconceived opinion, rarely a weariness, are the causes of these astonishing mistakes."

Face.—The subjects of aneurism are generally robust, vigorous-looking young or middle-aged men, with what is sometimes called the cardiovascular facies. Marked suffusion of the face is common when the aneurismal sac presses on the veins near the heart. The conjunctivæ may be dusky and infiltrated, and occasionally there is cyanosis. These features of venous compression are not, however, so common in aneurism as in tumor. Occasionally the congestion of the veins may be unilateral.

Inspection of the face gives us the interesting features supposed to be associated with pressure on the cervical sympathetic. Of these, inequality of pupils, *anisocoria*, is the most common. This is present in a very considerable number of cases, and may be due to three causes: (1) When the cord of the sympathetic in the neck is irritated there is contraction of the pupil on the affected side; when there is complete paralysis there is dilatation. Associated phenomena of sympathetic irritation are flushing, unilateral sweating, and drooping of the eyelid. (2) Cecil Wall and Ainley Walker¹ have brought forward evidence to show that this anisocoria is due more often to local vascular conditions. The size of the pupil is influenced very largely by the state of turgescence of the vessels. With low blood pressure, large pupils, with a high pressure contracted pupils, are associated; and these authors think that the anisocoria in aneurism is associated with unilateral change in the blood pressure. In 26 consecutive cases of inequality of the pupils in thoracic aneurism they found that there was nearly always a relation between

¹ *Lancet*, 1902, ii, 68.

the state of the pupils and the arteries. Where the temporals or radials were small the pupil was large. Experimentally, too, they found that obstruction of carotid vessels in the neck was always associated with a large pupil. In one case of aneurism at the root of the neck on the right side, in which the pupils were equal, distal ligature of the common carotid was followed by enlargement of the right pupil, and an operation on the carotid is reported in which this same sequence followed. In the majority of individuals, pressure on the carotid on one side is followed by enlargement of the pupil. This study gives a very rational explanation of the phenomenon, and removes a very serious difficulty, namely, that very often pupil changes are found when anatomically the aneurism has no connection whatever with the sympathetic. (3) In a certain number of the cases the inequality of the pupils is a syphilitic manifestation associated with the Argyll-Robertson phenomenon and absent knee-jerks, described as the Babinski syndrome.¹

Inspection of the neck may show great engorgement of the face on one or both sides, absence of the carotid pulsation on one side, sometimes enormous distention of the right jugular sinus, and in the aneurism of the arch or of the innominate arch together, pulsation of the tumor itself is visible just above the sternum or the sterno-clavicular joint. An interesting feature sometimes seen is the visible *tracheal tugging*, a systolic retraction of the box of the larynx, and of the tissues of the root of the neck along the line of the windpipe which may show a lateral deviation.

Arm and Hand.—Sometimes there is swelling of both upper extremities. Particularly is this the case in the aneurism of the ascending aorta, which had grown to the right and compressed the superior vena cava. Much more commonly the arm on one side is congested with enlarged veins, less commonly cyanosis. Pallor and sweating may be present in one arm only. A very interesting feature is unilateral clubbing of the fingers in thoracic aneurism. It is associated with peripheral stasis.

Skin of Chest.—Distention of the veins over the shoulder and pectoral region is common. A network of distended veins may be marked on the right side above the third rib. Very great enlargement of the mammary veins is not so often seen in aneurism as in tumor compressing the superior vena cava. The whole front of the chest may be occupied by large plexus of vessels communicating with the epigastric veins and all the well-known features of obstruction to the blood entering the auricle from above.

Pulsation.—Three sorts of pulsation may be seen in the chest: (a) A general shock, such as is present with violent throbbing of the heart, of an aneurism, or of a pulsating aorta. In great hypertrophy of the heart and dilatation of the vessels with marked anemia, the front of the chest is lifted and jarred with each impulse, often the subclavians throb, and there is a pulsation in the suprasternal notch. Even without organic disease of the heart, as, for example, in cases of Graves' disease, neurasthenia, and severe anemia, this diffuse throbbing, particularly when

¹ *Bull. et Mem. d. l. Soc. Med. d. Hôp.*, 1901, 18, 1121.

associated with marked pulsation of the subclavians, may lead to the diagnosis of aneurism. The shock may be so pronounced as to jar the bed.

(b) A diffuse impulse localized over certain parts of the chest and quite different from the general thoracic shock. Usually limited to one side of the chest, to the right mammary or subclavicular regions, it may occur, as is well known, with pleural effusion, gaseous or liquid. There are remarkable instances in which this diffuse pulsation of one side of the chest has occurred without any very obvious cause. This throbbing may occur in anemia and be most deceptive, as in the case reported by A. R. Edwards, in which over the lower left chest there was a diffuse pulsation extending horizontally from the angle of the left scapula into Traube's space and the epigastrium—"the pulsation was vigorous and distinctly expansile to both the eye and the hand." A systolic bruit was heard over it. Naturally the case was regarded as one of aneurism of the thoracic aorta. The postmortem showed moderate arteriosclerosis of the aorta, but no aneurism. Lafleur reports a very similar case with pulsation in the same region, and in addition paralysis of the left vocal cord. And lastly, in chronic *mediastinitis* there may be a most deceptive pulsation simulating that of aneurism. In 1902 there was under the care of the senior writer for some months, a patient aged fifty-nine years, who had increasing dyspnea, cough, and some pain in the chest; the fluoroscope showed an indefinite shadow to the left of the sternum. The voice was a little cracked, the arteries were thickened, and in the second right interspace extending toward the axilla was seen a diffuse impulse, very indefinite, when the breath was held. With the other symptoms and a slight tracheal tugging, naturally a diagnosis of aneurism was made. W. T. Howard, who made the postmortem, found chronic *mediastinitis*.

(c) *The punctate, heaving, true aneurismal impulse*, which is of a totally different character, localized, and when of any extent visibly expansile. It is first of all most important to recognize the regions in which the cardiovascular impulses may be visible. The apex beat in the fifth interspace and an impulse of the right ventricle in the left costoxiphoid angle are seen over the hearts of thin-chested, healthy persons. Other impulses which must not be mistaken for aneurism are the following: (1) The throbbing of the conus arteriosus in the second left interspace—very common in young persons and in thin chests, and seen particularly well during expiration. (2) Pulsation of the heart in the second, third, and fourth interspaces, extending as far as the nipple line in cases of sclerosis and retraction, from any cause, of the upper lobe of the left lung. (3) Heart pulsation in the second, third, and fourth right interspaces in connection with similar conditions of the right apex. (4) Effusion in either side of the chest may so dislocate the heart that there is a marked impulse at or outside the nipple line on either side. (5) Throbbing subclavians seen in the outer half of the infraclavicular regions, usually bilateral; this is met with in thin-chested persons, in neurasthenia, in early tuberculosis, and in anemia. Sometimes it is unilateral, and when accompanied with a thrill and

murmur it may form a mimic or phantom aneurism. Samuel West¹ has reported 8 cases of this kind. (6) In the back part of the chest visible pulsation is nearly always aneurismal; but occasionally, in Broadbent's sign the tugging may be so limited and localized in one interspace that it simulates pulsation, but palpation corrects this.

Palpation.—Over a blood tumor connected with the aorta and close to the heart, three things may be felt: (1) *The aneurismal impulse:* To appreciate its character one must understand that this is identical with the cardiac impulse, and to learn to recognize it one should practise carefully the palpation of an actively beating apex. The remarkable vigor and intensity, the impossibility of resisting it, the closeness under the fingers with the definite expansile quality, are its important features. These are only appreciated when the aneurism reaches the surface, but even when the sac itself cannot be palpated there may be communicated to the chest wall a forcible heave which is entirely different in sensation from the ordinary shock. In the deep-seated tumor beneath the manubrium this may sometimes be appreciated best by bimanual palpation—one hand upon the spine and the other forcibly compressing the sternum. The communicated shock or jar which is felt over the chest in a case of hypertrophied heart or a throbbing aorta is diffuse, without localization, without any punctate, heaving quality and without that sense of forcible expansion directly beneath the fingers which is so characteristic of the cardiac and the aneurismal beating. (2) Over the aneurismal sac near the heart may be felt the shock of either a thudding first sound or, what is much more common, the sharp flap of the second sound. The latter is of great diagnostic importance, and may sometimes be felt by the slightest application of the finger to the sac as a snapping, short shock. (3) *Thrill:* A marked vibratory thrill may be felt, usually systolic in character, much more rarely diastolic and not often double. Thrill is not a special feature of aneurism of the thoracic aorta, and a great majority of cases are without it. It is relatively more common in aneurism of the abdominal aorta. A diastolic thrill is exceedingly rare.

Tracheal Tugging.—When the sac is adherent to the windpipe, with each systole the larynx may be slightly drawn down, and if the finger be placed upon it, or if the windpipe is stretched, a slight tug may be felt. This very valuable sign, first described by Surgeon-Major Oliver, is present in a large proportion of all cases of aneurism of the arch when it is in contact with the windpipe. Occasionally it is present in great dilatation of the aorta and in tumors. It may be visible as well as palpable.

Inequality of the radial and carotid pulses is common. Usually the radial pulse on the one side may be slightly retarded or very much smaller. The carotid may be extremely feeble or obliterated, an event less common in this vessel than in the radial. The right pulse is more frequently smaller than the left. The inequality is most commonly due to involvement of the innominate in the sac with narrowing of its

¹ *St. Bartholomew's Hosp. Rep.*, 1880, 16, 119.

orifice. On the left side the subclavian, with or without the carotid, may be involved in the sac. Either subclavian may be compressed outside the sac. The radial may be smaller on the side opposite to that in which the sac is prominent. Thus a small radial on the left side with a projecting sac from the ascending aorta on the right side may be due to an atheromatous narrowing of the orifice of the left subclavian, or there may be a small secondary aneurism.

It was Harvey, I believe, who first noted the change of pulse in aneurism. In Chapter III of the *de Motu Cordis* he describes the following case: "A certain person was affected with a large pulsating tumor on the right side of the neck, called an aneurism, just at that part where the artery descends into the axilla, produced by an erosion of the artery itself, and daily increasing in size; this tumor was visibly distended as it received the charge of blood brought to it by the artery with each stroke of the heart; the connection of parts was obvious when the body of the patient came to be opened after his death. The pulse in the corresponding arm was small in consequence of the greater portion of the blood being diverted into the tumor and so intercepted."

The pulse may be imperceptible at the wrist and just felt in the brachial, or a very feeble impulse may be seen or obtained by the sphygmograph when nothing is felt by the finger. There are cases in which no pulsation is felt in any of the arteries of the head or of the upper extremities, generally instances of large aneurism of the transverse arch. It is much more rare to meet with obliteration of the pulse in the abdominal aorta or in the femorals. The writer reported one instance in which this interesting condition was present. Absence of the pulsation in a vessel does not necessarily mean that the orifice at the main trunk is obliterated. Feebleness of the pulse on one side may be due, as Harvey suggests, to the diversion into the tumor of the greater portion of the blood, and in the case of a very large sac the force of the cardiac systole may be entirely absorbed and an intermittent converted into a continuous stream.

Blood-pressure.—This may show variation in the two radials. O. K. Williamson¹ finds that while the arterial blood-pressure in aneurism is either normal or slightly above normal, in a majority of cases of thoracic aneurism there is a marked difference in the blood-pressure in the arms, and when this is greater than 20 mm. it is in favor of aneurism.

Percussion.—When the aneurism reaches the chest wall impairment of resonance shading to flatness is a common physical sign, detected most commonly to the right of the sternum, upon the manubrium, to the left of the sternum in the subclavian and mammary areas, and in the left interscapular region behind. When the sac is closely surrounded by lung the impairment of resonance may be very slight and only brought out on deep percussion. In large tumors the compression of the lung may lead to shades of tympanitic notes.

Auscultation.—Over an aneurismal sac what one hears will depend very greatly upon the degree of lamination with fibrin and the state of the aortic valves. Usually the heart sounds are transmitted loudly

¹ *Lancet*, 1907, ii, 1516.

into the sac, the first dull and thudding, the second clear, ringing, and accentuated, relatively louder, as a rule, than the first. This diastolic sound may be the only one audible, and when present is a very valuable diagnostic sign. Adventitious sounds are not always heard. It is surprising, indeed, in how many aneurisms a murmur is not heard. A systolic bruit is common, and it may be transmitted to the vessels of the neck. It may disappear or change in character, when the patient sits up (Corrigan's sign). "According to previous observations, confirmed postmortem, the harsher the bruit and the greater the thrill, the more nearly circular and the smaller is the opening in the aorta, provided the contents of the sac are mostly liquid blood" (Colt).¹ The diastolic murmur is less frequently heard, and is present when the aortic valves are insufficient or the ring dilated. Sometimes it is caused in the very large sac itself. A to-and-fro double murmur is not uncommon. A continuous humming-top murmur, with systolic intensification, is present when the sac has opened into one of the large vessels or communicates with one of the chambers of the heart.

A systolic murmur is not uncommon over the trachea, and it may sometimes be heard at the open mouth. (David Drummund).

State of the Heart.—Large sacs of the arch displace the heart downward and to the left, and cause it to assume a more transverse position in the chest. This is usually very well seen in the *x*-ray pictures. A very large aneurism growing downward may gradually dislocate the heart and occupy its position, as in the remarkable case reported by Gee. Aneurism of the descending thoracic aorta growing forward may flatten the heart somewhat and give a widespread and very diffuse sort of pulsation in the cardiac area. With the coexistence of aortic insufficiency, dilatation and hypertrophy of the left ventricle are present, and associated conditions, such as arteriosclerosis of the small vessels and contracted kidneys, may cause hypertrophy. But, as a rule, the heart is not enlarged in aneurism of the aorta. Yet occasionally, without any obvious reason, the heart may be voluminous.

Symptoms.—*Of aneurism of the aorta in general:* In many cases the condition is *latent*. Those who have seen much medico-legal work appreciate the great frequency of sudden deaths from this cause in apparently healthy individuals. The latent aneurisms are the small, rapidly growing sacs in or just above the sinuses of Valsalva. The small, dissecting aneurisms with rupture, more rarely the ordinary aneurism of the arch, reach a considerable size without symptoms or physical signs. It seems scarcely credible, and yet an aneurism of the arch may penetrate the chest wall and form a tumor the size of the top of a lemon without the patient suffering any serious inconvenience.

The symptoms and physical signs of thoracic aneurism are to a certain extent antagonistic. A patient with the most characteristic physical signs may have no symptoms; one with every symptom may have no physical signs. Hence, Broadbent's useful division into *Aneurism of Symptoms* and *Aneurism of Physical Signs*. As a rule, both features

¹ *Brit. Jour. Surg.*, 1925, **13**, 109

are combined. The symptoms may be considered under the three groups, functional, symptoms caused by compression, and certain special features.

(a) *Functional*.—A sac of moderate size interferes little, if at all, with the work of the heart, so that enlargement does not necessarily occur, and when present is usually the result of aortic insufficiency, relative or valvular. Palpitation of the heart, and irregular, unpleasant throbbing may be complained of. During a sudden exertion fainting may occur. Disturbances in the functions of the organs, due to lack of blood supply, are not very common. One carotid may be obliterated without any cerebral disturbances. Hemiplegia, however, may occur. The senior writer never saw an instance in which imperfect blood supply to the upper extremities was associated with either paresis or intermittent claudication. But aneurism of the thoracic or abdominal aorta or its branches may be associated with intermittent claudication, and it was in a case of aneurism of the internal iliac that Charcot described first this condition in man.

The *pain* in aneurism is usually attributed to the stretching of the nerves about the aorta and on the sac, but it may be largely due to changes in the artery itself, which has a rich nerve supply. It was the first symptom noted by 63 of the 132 patients with thoracic aneurism under the senior author's care at the Johns Hopkins Hospital.¹ It was present in 104 cases, being of a very severe character in 61. Its absence was noted in 25. We know that local conditions in the intima may cause agonizing pain, particularly the plug of an embolus. The senior writer once went into a house for a consultation, a doubtful case, just as the young man had an embolism of the left femoral. He was howling in agony, and could not bear to have the spot touched. Thoma refers to the early pain in the chronic aortitis which leads to dilatation of the arch and attributes it to the involvement of the Pacinian bodies in the adventitia.

Alan Burns, too, called attention to the pain in arterial disease. Attacks of severe angina pectoris may occur in the early stages of aortic aneurism. The cases are met with in comparatively young men who have had syphilis, and the paroxysms may be of great severity and of frequent recurrence. The physical signs may be negative, and it may be a year or more before aneurism is suspected. In other instances there are well-marked signs of aortic insufficiency. A feature of very great interest in certain of these cases is the complete disappearance of anginal attacks with the use of iodide of potassium.

(b) *Symptoms of Compression*.—An aneurism may grow to a large size without causing inconvenience. Whether active symptoms of compression are caused depends on the situation of the tumor and on the direction of its growth. From the ascending and terminal portions of the arch tumors extending laterally are much less likely to interfere with neighboring structures, and the largest tumors arise from these portions. The space between the posterior wall of the sternum and the spine at the level of the aorta is so small that aneurisms of the transverse portion of the arch cause early signs of compression.

¹ Osler, W.: *Med. Chronicle*, Manchester, 1906, 44, 69.

The chief symptoms of aneurism are those of tumor, and arise from interference with neighboring parts by compression. The following are the more important structures involved: (1) *Nerve trunks and plexuses*: Pain due to stretching and pressure on the nerves is a common yet a very variable feature. A huge sac may erode the chest wall without causing any serious inconveniences. The pain presents very different characters. As already mentioned, there may be attacks of angina pectoris associated with an aortitis, and the beginning of the formation of the aneurism. More commonly, it is of a dull, heavy character, deep seated, and greatly aggravated in certain positions. It may present the features of a cervico-brachial neuralgia; in other cases, of an intercostal neuralgia of great severity and persistence. Sometimes the pain shoots down the arm, and there may be numbness and tingling as far as the finger tips. Erosion of bones is usually associated with pain of a very intense boring character, but the sternum and adjacent cartilages and ribs may be eroded and perforated without causing distress. On the other hand, the spinal column when compressed is a source of persistent and terrible pain. Sometimes it is of the well-marked character of nerve-root pains, but in other cases it is a deep-seated, boring intense agony only relieved by maximum doses of morphine. These terrible tragedies of pain are most common in aneurism of the lower thoracic and abdominal portion of the aorta. The corresponding skin areas of Head may be sensitive to touch, in the region of the nipple, along the left sternal border, and over the neck.

Compression or irritation of certain nerves may cause special symptoms. Irritation of the *phrenic* may be associated with hiccough. Symptoms arising from compression of the pneumogastric are not often met with. Some have attributed to this cause the attacks of nausea and vomiting which occasionally occur, and the recurrent dyspnoea, but this does not seem to be very likely.

Pressure on the *sympathetic* does sometimes occur with the characteristic features, namely, flushing of one side of the face with increased heat, sweating, dilatation of the pupil, and slight drooping of the eyelid. This is, however, a rare combination. It has already been mentioned that the difference in size of the pupils is most frequently a question of tension in the ophthalmic arteries. Unilateral sweating is probably the most characteristic sign of compression of the sympathetic. This interesting feature, first noted by Gairdner, is usually confined to the sides of the face and neck, toward which the aneurism projects, and more frequently on the right side than on the left. It may occur on the side opposite to that in which the aneurism is bulging, but it is not always possible to say how far the sac may extend on either side of the middle line, and it is a very short distance from the aorta to the cord of the sympathetic. The sweating may extend to the arm and side of the chest and the skin of the right hand may be like that of a washerwoman's. Instead of being flushed and of a higher temperature, the skin on the affected side may feel cold and be several degrees lower than the opposite side. The skin of the face may look pale, and sometimes the hand and arm of the affected side are quite pallid,

The Recurrent Laryngeal Nerve.—Pressure on this nerve is a common event in aneurism of the arch, around which the left nerve curves, and it may occur with very small tumors. The right nerve may be involved in a large sac springing from the ascending aorta and the transverse arch. The symptoms caused are very important: (a) Alteration in the voice, which has a cracked character; sometimes the change is very slight, but in others it is most striking. Actual aphonia is rare, although the voice may be reduced to a whisper. Most commonly the voice is that of a unilateral paralysis. (b) A peculiar quality of the cough, which becomes ringing, “brassy,” or croupy. It differs from the cough of tracheal or bronchial compression, which is dry, harsh, and grating, and is usually accompanied with dyspnœa. (c) In rare instances there is painful spasm of the muscles of the larynx and pharynx, and even of the œsophagus. (d) Attacks of dyspnœa, which may occur with unilateral paralysis, are more common when both nerves are affected, as they may be by two aneurisms, or in rare instances by an ascending neuritis and extension to the nucleus of the other nerve.

Œsophagus.—Dysphagia is a very common and, with the small tumor from the posterior part of the arch, an early symptom. It is rarely extreme, but it may prevent the patient from taking solid food. Perforation of the œsophagus and fatal hemorrhage may occur without any previous difficulty in swallowing. The results of the compression may be necrosis of the wall without perforation. Ulceration may occur over the point of greatest compression. When the sac perforates directly into the gullet there is fatal hemorrhage; sometimes the orifice is temporarily blocked by a clot.

Trachea and Bronchi.—The most common and characteristic features of aneurism are associated with irritation and compression of the air passages. The condition may at first be mistaken for asthma. *Cough*, one of the earliest symptoms, is due in a great many cases to tracheal irritation, more particularly when the sac is in the neighborhood of the bifurcation. When there is simple compression, anything that lowers the tension in the sac benefits the cough, and ten days in bed may cause its disappearance. On the other hand, the slightest exertion may bring it on. In other cases the cough is due to a tracheitis, and the mucous membrane is found swollen and reddened and there is a great increase in the secretion. There is a difference in the character of the cough in the two conditions. In one it is dry and wheezing, nothing is brought up, but in the other there is a very large amount of expectoration. The peculiar, brazen quality of the cough in aneurism is laryngeal not tracheal.

Dyspnœa.—Aneurismal dyspnœa presents the following characteristics. In the first place there may be the ordinary shortness of breath associated with the growth of a large intrathoracic tumor, but without any signs of direct compression of the trachea. Aneurismal dyspnœa resulting from this cause is infralaryngeal and all grades are met with. In the aggravated cases there is an orthopnœa with prolonged inspiration, often noisy, sometimes with a marked stridor, or a fine sibilant sound. Expiration is shorter and not so noisy. While the

difficulty of breathing is constant, there are paroxysms in which the intensity is greatly increased and the patient feels, as Morgagni expresses it, as though a cord was being tightened about the wind-pipe. Retraction of the tissues at the root of the neck, the epigastrium, and the costal borders is usually present. Gerhardt called attention to the limitation of vertical movement of the larynx in tracheal stenosis: "In spasmodic and stridulous breathing laryngeal movement of less than one centimeter is a certain sign of tracheal or tracheo-bronchial stenosis." Very often these patients are admitted to the hospital in terrible paroxysms, and it may not be easy to determine whether the narrowing is laryngeal or not. If a laryngeal examination can be made it is not difficult, but otherwise it is not at all easy. The cracked voice, the brazen character of the cough, the quality of the stridor, whether over the larynx or lower in the course of the trachea, the degree of movement of the larynx in inspiration, are important points.

Compression of Bronchus.—An aneurism may narrow one or other main bronchus without seriously compressing the bifurcation, or only the branch going to one or other lobe may be involved. This may produce a picture in which the true nature of the disease is obscured. In gradual compression the condition of atelectasis may follow with subsequent sclerosis. This does not often happen to an entire lung, but it may to a lobe or part of a lobe. The narrowing results in retention of secretion and intense bronchitis, sometimes with expectoration of large quantities of muco-pus. Dilatation of the bronchi may supervene, but more common and deceptive is the gradual invasion of the lung tissue itself, so that the organ becomes consolidated, the bronchi filled with pus, sometimes quite inspissated, and the lung infiltrated, perhaps here and there a cavity formation. The whole process resembles tuberculosis, for which the cases may be mistaken.

Lung.—The growing sac may push aside the lung and compress the upper lobe without causing anything more than slight atelectasis, expressed clinically by the very important physical sign of feebleness or absence of breath sounds. But the sac may grow directly into the lung, the tissues of which form its actual wall. Under these circumstances, if the sac is small and grows from the terminal part of the arch into the left apex, and if hemoptysis is present, the case is of course mistaken for one of tuberculosis. The senior writer saw two such instances in 1907, one at the Royal Victoria Hospital, Montreal, with John McCrae, the other at the Radcliffe Infirmary, Oxford, with Dr. Mallam. In neither was there any suspicion of aneurism. In both there was fatal hemorrhage. In other instances the aneurism grows into the lung, and in the formation of a large sac repeated small hemorrhages occur. Complete consolidation may follow. There is a specimen in the McGill Museum of an aneurism which occupies a large portion of the centre of the left lung, and which had become obliterated by thrombi.

Bloodvessels.—Considering how close in many cases the aneurism is to the great veins, it is surprising how rare are severe symptoms due to compression of the superior vena cava. The pressure may be exerted on the vena cava itself, on the innominate, or on one of the subclavian

veins. It is not very uncommon to meet with congestion of the veins of the neck and head, and sometimes one or other arm is swollen. All this may disappear completely after a copious bleeding or after a week's rest in bed. The small aneurism of the ascending portion of the aorta growing to the right may compress the vena cava very early, even before physical signs are apparent. It is in this situation particularly that the most marked effects of compression from aneurism are seen. Narrowing of the lumen is the most common event, and throughout the course of the disease there is more or less fulness of the veins of the head and upper extremities. Rupture of the aneurism into the superior vena cava is followed by remarkable signs and symptoms, which will be discussed under the section of arteriovenous aneurism. The gradual compression may lead to thrombosis and complete obliteration of the superior cava. Of 29 cases which the senior writer collected in a paper¹ on obliteration of this vein, 4 were associated with aneurism. The picture is usually a very striking one, owing to the enormous development of the collateral circulation. This is carried on through a number of channels: (1) If the obliteration is above the point of entrance of the vena azygos, a large amount of blood from the arms and trunk finds its way into this vein through communications of the intercostals with the internal mammaries. (2) Over the surface of the chest the plexus of mammary veins enlarges and the subcutaneous tissues may be swollen, and the entire front of the chest is occupied by a system of greatly distended veins. These may be seen in and beneath the skin forming tortuous channels the size of the finger and converging to two or three large vessels which unite with the epigastrics. On the front of the abdomen are seen large convoluted vessels which empty below into the femoral veins. In some cases the venous plexuses are entirely subcutaneous. In others the veins of the skin itself are dilated and give the general surface a purplish-red hue. So distended may the superficial mammary veins become that in the large sinuses thrombi form which may ultimately calcify, forming vein-stones. (3) Extensive communications exist between the deep cervical and the vertebral veins with the intercostals and the whole network of veins along the front of the spine. These communicate freely with the branches of the azygos, or when the orifice of that is obliterated numerous channels are established between the lumbar vessels and the territories of the inferior vena cava.

The *inferior cava* is less often compressed. The *innominate vein* or *one subclavian* may be narrowed, rarely obliterated, causing great engorgement of the hand and arm. The *pulmonary artery* may be narrowed or perforated. Gangrene of the lung has been caused by compression of the vessels. *Compression of the vena azygos* may cause œdema of the chest wall or effusion into the right pleura. The *thoracic duct* may be involved in any part of its course, but symptoms due to this complication are rare. Morgagni noted the great dilatation of the abdominal lymph vessels with varices and lacunæ in a case of thoracic aneurism.

Spinal Cord.—In a few instances the bodies of the vertebræ have been destroyed and the spinal cord directly compressed by the sac,

¹ Bull. Johns Hopkins Hosp., 1903, 14, 169.

causing paraplegia. Rupture has occurred into the spinal canal. The paraplegia may be due to blocking of the aorta, which causes anemia of the cord such as follows ligation of the vessel experimentally.

Special Symptoms.—*Hemoptysis.*—Latent tumors growing backward from the transverse arch may rupture into a bronchus or the trachea, causing early and fatal hemorrhages. More frequently there are well-marked signs, and the bleeding may be of very different characters. With pressure and a granular tracheitis, bloody sputum may occur for weeks and gradually disappear. Brisk hemorrhage almost always comes from an open erosion, but it is not necessarily directly fatal. The laminæ may be within the lumen of the trachea, and through small chinks and crevices the sac may “weep” at intervals, or continuously for weeks and months. There are remarkable cases in which in the course of a few weeks numerous hemorrhages occur. Death may not follow for months or even years. A patient of Dr. Fussell, with aneurism, upon whom the senior writer lectured in Philadelphia, lived for four years after a severe hemoptysis. The famous surgeon, Liston, had, in July, 1847, a feeling of constriction at the top of the windpipe and slight difficulty in swallowing. A profuse hemoptysis, 30 to 40 ounces, nearly killed him. Liston himself suspected aneurism, but neither Watson nor Forbes could discover anything in his chest. He was greatly relieved by the hemorrhage. In October the symptoms returned, but it was not until December 6 that he died in a paroxysm of dyspnoea. The trachea was perforated, but the orifice was blocked by firm laminæ of fibrin. The small tumors growing upward into the apex of the lung on either side may be associated with repeated hemorrhages, and the diagnosis of tuberculosis is usually made.

Modes of Perforation.—1. *External.*—As the sac enlarges, the wall of the thorax is perforated, the tumor appears beneath the skin, and may reach an enormous size. Finally the skin becomes reddened, a spot of necrosis forms, slowly increases, the aneurism at first “weeps,” and finally bursts with fatal hemorrhage. Considering the large number of cases in which the chest wall is perforated and the skin eroded, fatal hemorrhage from this cause is comparatively rare. The sac may be very voluminous, as represented in Fig. 100, which shows a negro with an aneurism of the descending thoracic aorta. Lined as it is with firm thrombi, the sac may perforate the skin without any hemorrhage, and the patient may live for months and die of internal rupture. William Hunter reports the case of a man with an aneurism perforating to the right of the sternum, in whom the sac bled for weeks at intervals from an orifice plugged by a coagulum which protruded and retracted with the systole and diastole of the heart. A sudden cough burst out the plug, and “the blood gushed out with such violence as to dash against the curtain and wall, and he died not only without speaking but without a sigh or groan.” The senior writer has seen a sac “weep” for months; in one patient it became infected with the *Bacillus capsulatus aërogenes*, and the patient died of a general infection. It is remarkable how much a sac presenting externally may vary with the condition of the patient. Prolonged rest in bed, bleeding, wiring, may reduce the size, and we have had instances

in which the external tumor has completely disappeared. Great relief may be obtained by a carefully adapted bandage, but it must not be too tightly applied. By far the most common site of external perforation is to the right of the sternum. A prominent sac may disappear completely after external rupture (Morgagni). External rupture occurred in 61 of 1197 cases of rupture (Boyd).

FIG. 100



Aneurism of the descending thoracic aorta. (Photograph taken by I. C. Skinner, M.D., of Selma, Alabama.)

2. *Perforation into the Trachea or Bronchi.*—This occurred in 171 cases of rupture. It usually takes place in the lower third of the tube, and the orifice may be single or double. By pressure the wall is gradually eroded; a small, rapidly growing sac may perforate before there have been any special symptoms; more commonly there is an irritative cough and the characteristic dyspnoea. As already mentioned, the perforation is not necessarily fatal, and the symptoms may be, as in Liston's case, greatly relieved by the hemoptysis. The orifice may be closed by firm thrombi, and months or even years may elapse before final perforation takes place. In one case under the care of the senior writer there were two perforations, and the patient died of a third one into the œsophagus. The left bronchus is more frequently involved than the right, more frequently, indeed, than the trachea itself.

3. *Rupture into the Lung.*—The lung tissue itself may form a large part of the wall of the sac, and it is particularly aneurisms of the terminal portion of the arch and the first part of the thoracic arch that tend to

grow into the upper lobe or invade the central portion of the lung. Slight and recurring hemoptysis may occur, and the diagnosis of tuberculosis is sometimes made. The writers have not met with an instance of fatal hemorrhage unless the sac opened into a bronchus. There may be a very large sac almost completely consolidated within the lung substance.

4. *Œsophagus*.—There were 112 cases among 1197 ruptures. The rupture takes place usually by gradual erosion, which has sometimes been preceded by local necrosis and gangrene. Dysphagia usually precedes the perforation, but in small sacs the rupture may take place suddenly in individuals in excellent health. Such an instance occurred in a woman, aged thirty-five years who died in syncope. The aneurism was only 5 by 5 cm. in extent, and communicated by a linear slit 1.5 cm. in length with the lumen of the aorta. It is not uncommon to find the *œsophagus* stretched over the wall of the sac, closely adherent, and the muscular layers much wasted. The cases in which ulceration and gangrene precede the rupture are of special interest, since cancer of the *œsophagus* may be suspected. It may take place simultaneously into the bronchus or trachea and the *œsophagus*. The coats of the *œsophagus* may be split and the blood pass between them and burst into the stomach, as in a case reported by Frederick Taylor.

5. *Rupture into the Pericardium*.—This is one of the common causes of sudden death in robust, apparently healthy men. Medico-legal records of large cities show the very great frequency of this accident. This occurred in 369 of 1197 ruptures. The perforation may be of a small sac of one of the sinuses of Valsalva, or there is a tear of the intima with a small dissecting aneurism and rupture of the external coat, or the intra-pericardial portion of an aneurism of the ascending portion of the arch gives way. The rupture may be pin-point in size or a large transverse tear. In a few cases a small mycotic aneurism bursts. Death takes place with suddenness. There are instances on record in which the patient has lived for some hours.

6. *Other modes of rupture* are into the pleura (264 of 1197 ruptures) into the stomach, into the anterior or posterior mediastinum, the muscles of the neck, and into the vessels and heart.

The conditions under which rupture may occur are important. When the individual is at rest or sleeping the fatal event may happen. More often the rupture is during some exertion, while straining at stool, or in a scuffle, or while under an anesthetic. The dangers of coitus were referred to by Morgagni, who says that many patients die in this way.

Pleura.—Hydrothorax is not very uncommon, and may be a pressure effect on the azygos veins, and it is more frequent on the right side than on the left. It may complicate the diagnosis, and sometimes recurs repeatedly. The bloody serum may be present as an effect of pressure on the veins. Acute pleurisy, usually tuberculous, may be a terminal event. In a few cases aneurism has been complicated by empyema.

Descending Thoracic Aneurism.—Aneurism of this portion presents a few special features. It is rarer than in the abdominal aorta. If we add the statistics of Crisp, Lebert, and Myers, this portion was involved in 40 against 159 of the ascending, 113 of the arch, and 83 of the abdominal

aorta. It was involved in only 3 out of 64 cases of aneurism of the aorta among 2200 autopsies at the Johns Hopkins Hospital. Chaliel¹ in 1923 collected 69 cases from the French literature and gives a very detailed review of the main symptoms of aneurism of the descending thoracic aorta.

Symptoms.—There may be no symptoms whatever; the first indication may be a sudden syncope from internal hemorrhage, vomiting of blood or hemoptysis. Three of 14 cases described by the senior writer² were latent. A second feature is the intensity and the peculiar character of the pain. Owing to the close relation of the aorta to the spine and the frequency with which the tumor grows backward, pain in the back and along the sides from pressure on the nerves is usually *the symptom* of the case. Erosion of the spine to an extensive degree may occur without pain, but this is rare. Some of the patients are never without it for a moment, except when under the influence of morphine, of which one patient took for a long period as much as between 30 and 40 grains a day. There may be nothing in the case but the *pain*. Perhaps to the left of the spine there is heard a soft systolic murmur, or there are feeble breath sounds in the left lung, but it may be months before there are any physical signs. The third special feature is the prominence of the pulmonary symptoms due to pressure either on the lung itself or on the main bronchus. Hemorrhage occurred in only 3 of 14 of the senior writer's cases; it may be due to a direct weeping through the lung tissue, or it is a terminal hemoptysis due to perforation of a bronchus. The whole lung may be compressed by an enormous aneurism, or the bronchus may be blocked with the production of purulent bronchiectasis, and the patient may present the symptoms of extensive destruction of the lung or in slight compression, the inspiratory murmur may be normal the expiratory interrupted. Some writers have referred to pressure on the gullet as a special feature of aneurism of this part. It was present in only 2 of the senior writer's cases and in only 1 did rupture take place into the œsophagus. The tumor may grow to an enormous size, as in the famous case³ in which the patient lived for twelve years and the greater part of the left chest was occupied by a non-pulsating tumor.

Abdominal Aorta.—The *incidence* varies in different localities. Sixteen cases occurred among about 18,000 admissions to the senior writer's wards. The ratio of abdominal to thoracic aneurism was 1 to 10. Among 2200 autopsies at the Johns Hopkins Hospital there were 11 instances of aneurism of the abdominal aorta. The Guy's Hospital figures were collected by the late J. H. Bryant⁴ for the years 1854–1900; among 18,678 necropsies, there were 325 cases of aneurism of the aorta, of which 54 (or 16 per cent.) were of the abdominal portion. Among 17,872 postmortems at St. George's Hospital during a period of sixty-five years Nunneley⁵ was able to find but 32 cases: these give a good idea of the comparative rarity

¹ *Rev. de Méd.*, 1923, **40**, 65.

² *International Clinics*, Phila., 1903, 13th series, **1**, 1.

³ Sokolowski: *Deutsch. Arch. f. klin. Med.*, 1877, **19**, 623.

⁴ *Clinical Jour.*, London, 1903, **23**, 71; 89.

⁵ *Aneurism of the Abdominal Aorta*, 1906, London (Ballière, Tindall & Cox).

of abdominal aneurism. J. A. Nixon¹ in 1911 gave a good epitome of 233 cases collected from the literature, and reported a case occurring in a girl, aged twenty years, the subject of congenital syphilis. Marlow and Doubler² in 1918 found 11 additional cases and contributed 2 cases of their own. Males are much more frequently attacked than females. Only 2 of the senior writer's 16 cases were females, and all statistics indicate this infrequency in women, a point to be borne in mind as the throbbing aorta is so much more common in them. A majority of the patients are young men. In 63 per cent. of Bryant's series they were under forty years of age, and in 2 the disease began before the twentieth year.

It is most frequent in the upper portion of the abdominal aorta, and it is usually of the saccular form. Rupture into the retroperitoneum is common, forming the diffuse or false aneurism, which may reach a colossal size. Rarely it may rupture into the gastro-intestinal tract as it did in 7 of the 246 cases collected by Nixon, Marlow and Doubler. A huge sac may occupy one-half of the abdomen and project in the back, forming a tumor the size of the head.

Symptoms.—In no situation are the symptoms of aneurism so obscure, and even when pulsation is present the diagnosis is not easily reached. This is well brought out by Bryant in the analysis of the Guy's Hospital statistics: "A correct conclusion during life as to the nature of the disease was arrived at in 18 only out of the 54 cases on which this lecture is based, an analysis showing that an abdominal tumor was detected in 31, pulsation in 35, expansile pulsation in 8 only, and in 26 a systolic murmur. Incorrect diagnoses of a variety of diseases were made, including malignant tumors lying in front of the aorta, renal calculus, lead colic, spinal caries, sarcoma of the kidney, nephritis, perinephritis, pneumothorax, pleuritic effusion, epithelioma of the œsophagus, malingering, chronic intestinal obstruction, etc."

Pain, usually the first indication, remaining throughout the special feature and reaching an intensity not met with in any other disease, presents three features of importance. It is usually of a constant, dull, boring character, particularly when the aneurism has eroded the spine. There may be paroxysms of the greatest intensity for months before a diagnosis is made. The pain may be segmental with hyperesthesia of the skin fields; there may also be transitory paresthesia in the lower limbs. And lastly, when the aneurism ruptures into the retroperitoneal tissues, the pain with other features may give to the case the characters of the acute abdomen. The senior writer knew of at least four cases in which the operation for appendicitis was undertaken. Nausea and vomiting may be early and severe symptoms. In one of the cases there was great dilatation of the stomach due to pressure upon the duodenum. In another there was great dilatation of the œsophagus owing to pressure at the cardiac end of the stomach; an aneurism of the hepatic artery may cause jaundice and intestinal hemorrhage. Compression of the splenic vein may cause enlargement of this organ. The aneurism may rupture into the stomach, duodenum, or colon, into the retroperitoneal

¹ *St. Bart. Hosp. Rep.*, 1911, **47**, 43.

² *Am. Jour. Med. Sci.*, 1918, **155**, 540.

tissues, which is the most common mode, or pass upward and rupture into the pleura. The peritoneum, the bladder, or the inferior vena cava may be perforated. Embolism of the aorta below the sac may occur, or one femoral may be blocked with the result of gangrene of the leg. The senior writer did not find a case of external rupture. Embolism of the superior mesenteric artery may occur with infarction of the bowel.

ARTERIO-VENOUS ANEURISM

A communication between artery and vein with or without an intervening sac. In the one case the term *aneurismal varix* is applied, and in the other, when a sac is formed between the two vessels, *varicose aneurism*. Although chiefly a surgical affection, met with in the peripheral arteries, it occurs in the internal vessels and has important medical bearings.

William Hunter, in 1757, described a particular species of aneurism following the simultaneous opening of an artery and a vein, in consequence of which the latter became dilated and varicosed, and had a pulsatile, jarring motion with a hissing noise. He described several cases which occurred from unskilful venesection at the bend of the elbow. The observation was not new; from the time of Galen it has been known the aneurism might follow unskilful venesection at the bend of the elbow, but Hunter recognized it as a special form. The monograph of Breschet¹ and the work of Broca² are of great value; indeed, there is not a better description in literature than that given in the latter.

Traumatic.—These cases have a surgical rather than a medical interest. While in the internal vessels the communication is usually direct, in the larger external trunks there is more often the intervention of a sac. Formerly, venesection at the bend of the elbow was the common cause, and the communication existed between the brachial artery and the vein. Now the cases are chiefly the result of stab wounds and of bullet wounds. Military surgeons state that with modern bullets the lesion has become more common. The experience of the South African War is given by W. F. Stephenson³ in a Government Report, and of the Russo-Japanese War by Saigo.⁴ The work of Matas⁵ and the technique in arterial surgery developed by Carrel⁶ led to greatly improved results in the World War. Makins⁷ and other British surgeons have published extensive papers on the vascular lesions produced by gunshot injuries, which were not only more severe than in former wars, but were also accompanied by more extensive destruction due to the use of the pointed rifle bullet and of high explosive shells and bombs. Makins gives a good analysis of the symptoms and treatment of 85 cases of arterio-venous aneurism and aneurismal varix.

¹ *Memoires de l'Academie de Medicine*, 1833, **3**, 101.

² *Des Aneurismes*, 1856 (Labé, Paris).

³ *On the Surgical Cases, etc.*, 1905, pp. 223-226.

⁴ *Deutsch. Zeit. f. Chir.*, 1906, **85**, 577.

⁵ *Jour. Am. Med. Assn.*, 1902, **38**, 103, et seq.

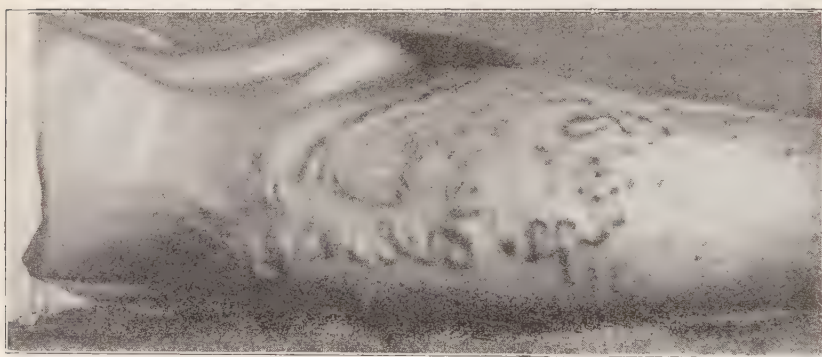
⁶ *Ibid.*, 1910, **54**, 141.

⁷ *Brit. Jour. Surg.*, 1915, **3**, 353.

The vessels most commonly involved are the femorals, subclavians, axillaries, brachials, and popliteals. So much higher is the arterial than the venous blood-pressure, that when an artificial communication exists between vein and artery, the former with its branches becomes permanently distended. The obstruction offered to the free return of blood makes the distention of the collateral veins still more marked. The orifice of communication may be small and slit-like or oval, and, as already stated, a sac may exist between the two vessels. In many cases the communication is direct. The anatomical changes are chiefly in the veins, which become greatly enlarged, varicose, with thickened walls, and frequently present flakes of atheroma in the intima.

The three distinguishing features of this aneurism are: (1) The swelling of the part caused by the distention of the veins. When only the deeper vessels are involved, they may not be visible externally, but, as a rule, large varicose vessels are to be seen. In the case of arteriovenous aneurism of the femorals or iliacs the engorgement of the veins

FIG. 101



Arteriovenous aneurism of the iliac vessels.

may be enormous. In no condition do we see such huge saccular dilations. In the annexed figure one of these is shown forming a large tumor just above Poupart's ligament. In the veins and in the large venous sinuses pulsation may be visible, but, except close to the arteries, it is not forcible. (2) On palpation a vibratory thrill is felt, of maximum intensity over the position of the orifice, but widely diffused, and in the case of an aneurism of the axillary vessels, to be felt as low as the palm of the hand, and in the case of an aneurism of the femoral vessels, to be felt as low as the foot, and even to the crown of the head. In the large bunches of subcutaneous veins, the calcified walls and occasionally phleboliths may sometimes be felt. When a sac intervenes between the artery and the vein, it may be felt, and presents aneurismal pulsation, forcible and expansile. (3) On auscultation there is heard everywhere over the aneurism and up and down the limb a "bruit de diable" of great intensity. An interesting point is the fact that one of the earliest instances recorded of auscultation was in a case of varicose aneurism

reported by Mr. White, a surgeon at York, in a letter to William Hunter. He states, "On applying my ear to the tumefied basilic vein, the pulsation, tremulous motion, and noise are distinctly perceived." The murmur is continuous, with systolic intensification.

The condition may remain stationary for years. Spontaneous healing does not occur. There may be progressive increase in the veins, leading to enormous varicosity and to great disability, and it is for this that relief is sought. This progressive enlargement of the veins is really the chief danger. At the age of fifteen years a young man fell and forced a lead-pencil into his axilla. This was followed by a gush of blood, and in a few moments the arm began to swell and became black and blue to the wrist. He gradually got better, but there was always a swelling in the armpit and infraclavicular region. It did not, however, interfere with his work or exercise. Ten years after, when the senior writer¹ saw him, he had well-marked signs of arteriovenous aneurism of the axillary vessels. He was athletic and had rowed in races. He subsequently served in the South African War, and was invalided for aneurism. He died thirty-one years after the accident of gradual heart failure. The autopsy revealed spontaneous healing of the orifice between the artery and vein.² Sudden death may occur either from heart failure or from embolism or from rupture of the sac. In the crural vessels, progressive disability may result from the varicose veins, thrombosis and ulceration. And lastly the vascular tissue involved in the aneurismal area may take on a nævoid growth. Broca mentions two interesting circumstances: the greater growth of the limb below a femoral aneurism of this kind, and the increased growth of hair on the skin, both the result of the venous engorgement.

Internal Arterio-venous Aneurism.—While rare, this form is of great interest.

1. **The Aorta and Superior Vena Cava.**—This gives a very remarkable picture. One morning, at the hospital of the University of Pennsylvania, a Chinaman, aged forty-eight years, was admitted in a condition of extreme dyspnœa, with the skin of the face and arms cyanosed, the eyes suffused, and the whole upper part of the body engorged and œdematous. He presented an extraordinary appearance on account of the contrast between the upper and lower part of the body. The senior writer had never seen a similar picture. The case, which was under the care of his colleague, Pepper, excited a great deal of interest. The most striking physical signs were: a loud thrill over the precordia, a continuous "humming-top" murmur, with marked systolic intensification, which was heard best over the base, and was transmitted into the vessels of the neck and down the arm as far as the elbow. The patient lived for two weeks, with extreme orthopnœa and an increase of the œdema of the upper part of the body; so intense was the infiltration of the blood-vessels of the conjunctiva that blood oozed. A small aneurismal sac of the ascending aorta had perforated the superior vena cava.³ A second case at the Johns Hopkins Hospital, in 1899, presented an almost identical

¹ *Ann. Surg.*, Phila., 1893, **17**, 37.

³ *Trans. Assn. Am. Phys.*, 1890, **5**, 45.

² *Lancet*, 1915, i, 949.

appearance.¹ The patient's face was enormously swollen and blue looking, like a man who had been strangled. There was the same extraordinary contrast between the upper and the lower part of the body. In the second right interspace was heard a loud, continuous murmur, with marked systolic intensification. The patient had had syphilis two years before, and although there were no signs of aneurism, there could be very little question as to the nature of the trouble.

The first report of a case of this kind was by John Thurman,² whose paper on these internal arterio-venous aneurisms was the first and is one of the best in literature. Pepper and Griffith collected 28 cases and others have been reported since their paper bringing the number to 47 (Fussell,³ Herrick,⁴ Anderson,⁵ Mayers⁶ in 1924). The symptoms are quite distinctive: (1) cyanosis, œdema, and distention of the veins of the upper part of the body, with signs of obstruction in the tributaries of the superior vena cava; (2) suddenness of the onset of the symptoms; (3) evidence of the presence of a tumor in the thorax; (4) the existence of a murmur characteristic of a communication between an artery and a vein.

2. **Aorta and Pulmonary Artery.**—This is rather more frequent, and the condition has been carefully studied by Frederick Taylor and Gairdner; Kappis,⁷ from Bäumler's clinic, has collected 30 cases. The latest review was in 1924 by Scott⁸ who collected 55 cases from the literature and added 2 of his own. Abbott⁹ recognizes two types: the first due to a congenital thinning of the septum between the two great trunks; the second, due to acquired disease of the aorta from syphilis and other infections, is by far the more frequent. The symptoms are not unlike those of perforation into the superior vena cava and are characterized by a sudden onset with cyanosis and œdema, which, however, are not so accurately limited to the upper half of the body, as in the cases of perforation into the superior vena cava. Signs are usually present of aortic aneurism. A thrill is felt over the base of the heart, and there is a loud humming-top murmur, with maximum intensity to the left of the upper part of the sternum. Thurnam has reported a case of perforation of an aneurism into the right ventricle, which had a murmur of the same character in the second left intercostal space.

Perforation of an aneurism into one of the branches of the pulmonary artery gives rise to a similar murmur. In a case admitted to the wards in 1901, with aneurism of the thoracic aorta, there was a feeble thrill and very loud continuous murmur occupying the entire cardiac cycle, with marked systolic intensification. This was heard best to the right of the sternum. The aneurism was found to have compressed the right lung, which formed the posterior wall of the sac into which one of the main branches of the pulmonary arteries had opened.

¹ *Jour. Am. Med. Assn.*, 1902, **38**, 1483.

² *Medico-Chirurgical Soc. Trans.*, 1840, **23**, 323.

³ *Trans. Assn. Am. Phys.*, 1906, **21**, 142.

⁴ *Am. Jour. Med. Sci.*, 1919, **158**, 758.

⁵ *Jour. Am. Med. Assn.*, 1923, **71**, 1877.

⁶ *Deutsch. Arch. f. klin. Med.*, 1907, **90**, 506.

⁷ *Jour. Am. Med. Assn.*, 1924, **82**, 1417.

⁸ *Contributions to Med. and Biol. Research dedicated to Sir William Osler*, 1919, **2**, 899.

⁹ *Ibid.*, 1924, **83**, 189.

3. **Abdominal Aorta and Inferior Vena Cava.**—This is not so common. Thurnam reports 3 cases in his paper, in all of which the perforation had taken place from an aneurism. In 1 case in J. H. Bryant's series at Guy's Hospital the vena cava was perforated. As a rule, the symptoms are well defined, namely, those of aneurism of the abdominal aorta with sudden onset of swelling and cyanosis of the lower extremities, and œdema of the lower half of the body. The characteristic humming-top murmur is heard over the tumor.

Diagnosis.—From **Dynamic Dilatation of the Aorta.**—That the throbbing, distended aorta, the condition of preternatural pulsation, as Allan Burns calls it, may lead to diagnosis of aneurism is an observation that dates from the time of Morgagni. It is met under the following conditions:

1. **Aortic Insufficiency.**—In young persons the degree of dilatation caused by the propulsion of a large volume of blood from a powerfully acting heart may be extraordinary. It is not very uncommon to see a slight throbbing of the aorta to the right of the sternum in these cases. Occasionally in a young man, when the insufficiency is extreme, and if anemia is present, the degree of throbbing and the extent of visible impulse in the second and third, or in the first and second right inter-spaces almost compels the diagnosis of aneurism; and yet postmortem the aorta may not be beyond the ordinary size. Much more commonly the mistake arises from the throbbing and dilatation of the innominate and the right carotid. Corrigan calls attention to this in his original paper: "So strong were the pulsations for years in the region of the arterio-innominate that until the examination after death there was never even a doubt expressed that the case was not aneurism." Many cases of this sort have gone into literature as aneurism. In 1886, Hare¹ reported an interesting case of this kind. A girl of seventeen had had repeated attacks of rheumatic fever, and she had been made the subject at several clinics, at which no doubt had been expressed as to the existence of aneurism. Nor is this to be wondered at when one reads Hare's statement: "There was an egg-shaped protrusion in the supra-sternal notch, very expansile and bulging with each systole of the heart, and the dilatation extended well up into the vessels." There was great hypertrophy of the heart, a double aortic bruit, and a Corrigan pulse. I had repeated opportunities to examine the patient; it was not a case of throbbing of the innominate and the right carotid during ventricular systole, but there was a prominent, dilated tumor to be grasped between the fingers just above the sternal notch. Having had a lesson in a somewhat similar though not so exaggerated a case, I had learned to be very chary in making the diagnosis of aneurism in young persons with aortic insufficiency. At the postmortem it was not a surprise to find the condition had been one of simple dynamic dilatation. The heart was enormously enlarged, there was an extreme degree of insufficiency of the aortic valves, the arch of the aorta *did not admit the index finger, nor the innominate the little finger*. It is important to bear in mind that there may be permanent fulness of the vessel, so that there is a tumor-like

¹ *Medical Record*, 1886, 29, 558.

dilatation left above the sternal notch or the right sterno-clavicular articulation. Many of the cases of so-called aortitis and aneurism in young persons following rheumatic fever are of this nature.

2. *Dynamic Dilatation in Neurotic Conditions.*—In hysteria, in neurasthenia, and in Graves' disease the throbbing vessels may lead to diagnosis of aneurism. It is not often that the dilatation and pulsation is of the arch. Bramwell, in his work on *Diseases of the Heart*, p. 723 has reported a remarkable instance in which "pulsation and dulness in the region of the heart were so distinct as to lead Dr. Murray, of Newcastle-on-Tyne, whose diagnostic ability generally, and in aneurism in particular, is well known, to believe that an aneurism of the ascending portion of the arch of the aorta was probably present." Within a few months these physical signs "completely disappeared."

It is more particularly in the abdominal aorta that the abnormal aortic pulsation leads to error in diagnosis. The subjects are usually neurotic, sometimes definitely hysterical. They complain of pain in the back and at the occiput, and have the usual symptoms of nervous exhaustion and debility, but the special feature upon which all their feelings centre is the throbbing in the abdomen, which may be so severe as to interfere with their sleeping or even with the taking of food. In extreme cases there are pain, shortness of breath, and even remarkable attacks of hematemesis. It is stated that Hippocrates had noticed this pulsation, but to Morgagni we owe the first accurate description. Allan Burns¹ gives a very careful account of the condition, and quotes from Albers, of Bremen, a remarkable instance in which, associated with the throbbing, there was passage of dark blood in the stools. The association of small hemorrhage from the stomach and intestines has been described by Sidney Phillips.²

The points to be borne in mind in these cases are: (1) That the pulsation occurs in nervous or hysterical women, or in neurotic or hypochondriacal males. In mild forms it is common. (2) The subjective sensations may be pronounced: pain, abdominal distress, nausea, sickness, constipation, and, in some instances, the vomiting of small quantities of blood and the passage of blood in the stools. (3) The degree of visible and palpable pulsation may be extreme. The abdominal aorta is easily palpable and may be grasped in the fingers. It is sometimes tender. No definite tumor is felt. With much anemia a thrill may be present. A soft systolic bruit may be heard, even without any pressure of the stethoscope. A mistake is not likely to occur if it is remembered that no pulsation, however forcible, no thrill, however intense, no bruit, however loud, singly or together, justify the diagnosis of an aneurism of the abdominal aorta, but *only the presence of a palpable, expansile tumor.*

3. *In Anemia.*—In extreme anemia from any cause the bloodvessels throb in a remarkable manner, and may suggest aneurism. This is not often the case in the thoracic aorta and its branches, but in the abdominal aorta it may be extreme. There are conditions, indeed, under which the diagnosis of aneurism seems definite. The senior writer has often referred to an interesting experience of this kind in a case seen in 1885 with Dr. Whiteside. A large, stout man, aged forty-five years, had had

¹ *Observations on Diseases of the Heart, etc.*, 1809, pp. 262-277.

² *Brit. Med. Jour.*, 1887, ii, 762.

for some months dyspepsia and pain in the abdomen. He had become very anemic, and the day before he was seen he had an increase of the pain. When examined he was sweating, pale, and the large, fat abdomen throbbed in a most extraordinary manner. The shock of the impulse was communicated to the patient's body, was visible everywhere from head to foot, and standing against the foot of the bed one could feel distinctly the jarring impulse communicated to it. On palpation the throbbing was violent with each systole, but it was trifling in comparison with the extent of visible pulsation. There was a loud systolic murmur, but no thrill. That evening he passed a large quantity of blood from the bowels and though a definite tumor could not be felt, it was thought that the diagnosis of aneurism was certain. The postmortem showed a duodenal ulcer placed directly upon the pancreas. The aorta was normal. In pernicious anemia in the vessels of the neck and in the subclavians the throbbing may be so violent as to suggest aneurism.

From Other Tumors.—These may be subcutaneous, of the chest wall, or internal. (a) *Subcutaneous*: It does not often happen that a tumor beneath the skin on the chest wall is mistaken for aneurism. The suspicious ones are associated with necrosis of the sternum and the formation of the cold tuberculous abscess. There may be communicated throbbing, more particularly if the abscess has lasted long and there is periostitis of the posterior part of the sternum directly over the aorta. There may then be a definite jarring which is visible in the tumor. The points of difference are, however, very clear. The abscess tumor is softer and there is not an expansile, forcible impulse. The shock of the heart sounds is not felt, and there is no murmur. More confusing are the rare instances in which the *empyema necessitatis* pulsates. Here, too, the projecting tumor between the ribs has not a strong, heaving, expansile pulsation, but it is a diffuse throb. Then the signs of empyema are usually very clear, and, if in doubt, the needle may be inserted.

The ruptured aneurism of the abdominal aorta may form a very large tumor in the back, or the blood may pass down and form a mass in either iliac fossa, which may be mistaken for abscess or for appendicitis. Nowadays, with the frequency of abdominal operations, the mistake is not uncommonly made. The writer knows of four instances in which under these circumstances operation was performed, thrice for appendicitis, once for supposed abscess. As already mentioned, in some of the very large diffuse aneurisms of the abdominal aorta there may be little or no pulsation. The older authors mention many instances in which aneurism was opened in mistake for abscess. Ambroise Paré mentions a case of a priest in whom a barber surgeon had opened an aneurismal sac, and the patient bled to death. Morgagni also gives a case. ¶

(b) *Of the Chest Wall*.—It does not often happen that a tumor of the chest wall is mistaken for aneurism. Osteosarcoma of the sternum or myeloma of this bone or of the rib may form a tumor to which a jarring impulse is communicated. A vascular osteosarcoma of the sternum may have a very deceptive pulsation of its own, but the senior writer never saw any such case and in pulsation of a rapidly growing tumor of the rib, the other circumstances left no doubt as to its nature.

(c) *Internal*.—Since the symptoms caused by an aneurism are those of tumor, it is not surprising that difficulties arise in mediastinal and other growths, but these difficulties have been greatly diminished with the aid of the *x*-rays. In two groups of cases error is possible. (1) The *small, solid growth* in the posterior mediastinum connected with the glands or with the œsophagus, which presses upon the windpipe, causing cough and orthopnoea and perhaps paralysis of the left recurrent nerve, gives a clinical picture identical with that of deep-seated aneurism. Nowadays even a very small aneurismal sac may be recognized with the *x*-rays. In a case of mediastinal tumor which gives only symptoms, that is to say, when there is orthopnoea and urgent distress, but nothing to be made out on examination by ordinary means, aneurism is much more likely than new growth. Occasionally the small tumor of the œsophagus is mistaken for aneurism. The statement is made that an œsophageal bougie, used for purposes of diagnosis, has been thrust into an aneurismal sac, but the writer has not found the record of such a case. The confusing circumstances are those in which there is difficulty in swallowing, attacks of dyspnoea, stridulous cough, and paralysis of the left vocal cord. When the œsophageal tumor is just at the bifurcation of the trachea it may form a small, hard mass involving the recurrent laryngeal nerve and causing great difficulty in diagnosis. An important point in the diagnosis of new growth is the age of the patient, which is more likely to be advanced. In the small tumor, whether of glands or gullet, the cervical lymph glands may not be involved.

The voluminous *intrathoracic tumor* growing from mediastinum, lung, or pleura may offer great difficulty. When situated over the aorta or over the heart, particularly to the left of the sternum, the communicated pulsation may be most deceptive, the heaving quite localized, and there is usually a bruit. There is never the strong expansile impulse, felt directly beneath the fingers, and upon this, not upon the extent of visible or palpable impulse, stress should be laid. With venous obstruction and the anterior wall of the chest œdematous and congested, the difficulty may be very great indeed, and the associated features of the case may be more helpful than any other. An enlarged gland above one clavicle or in the axilla, the mode of onset, the age, sex, the history of syphilis, are all important elements. The *x*-ray examination is most helpful in this group, as the outline of the pulsating aorta and heart may be differentiated from the lighter shadow cast by the tumor. Not all patients with aneurism give a positive Wassermann reaction.

On the other hand, the huge chronic thoracic aneurism may simulate tumor, as the lamination may be so dense that pulsation is absent. In a famous case,¹ Oppolzer diagnosed aneurism and Skoda tumor. The left half of the thorax was flat and there was no pulsation. The patient lived twelve years. The sac filled the greater part of the left chest. Aneurism and sarcoma may occur together, as in a case reported by Virchow in which the two were in direct connection.

From Other Forms of Pulsatile Tumors.—Not every abnormal pulsation indicates an aneurism. It may be well to mention the various forms of pulsatile tumors: (a) *Erectile tumors*: The diffuse angioma, in

¹ Sokolowski: *Deutsch. Arch. f. klin. Med.*, 1877, 19, 623.

which all the vessels, arteries, capillaries, and veins are involved, forms a red- or violet-looking tumor when the skin itself is involved (which is usually the case), but sometimes it is entirely subcutaneous. The pulsation is diffuse, and a bruit is heard over the tumor. (b) Cirroid aneurism, in which the arteries are chiefly involved; and in the recognition of this form there is rarely any difficulty. (c) Ordinary aneurism, true or false. (d) The arteriovenous aneurism. (e) The very vascular malignant tumors.

The last is the form of pulsating tumor which may be confused with aneurism. Rapidly growing tumors of bone and vascular sarcomata of the abdomen may present an expansile impulse, usually better felt than seen, but occasionally very marked on inspection. In two instances the extent and force of the pulsation led to error. One was a man with a large, rapidly growing sarcoma of the upper part of the thigh bone, in which the pulsation was so pronounced that the femoral artery was believed to be involved. The other was a large sarcoma, probably growing from the retroperitoneal glands, which had a forcible expansile pulsation, and a loud bruit could be heard. In the case of tumors of bone, either in the extremities or in the head, there should rarely be any difficulty; but the pulsating sarcoma in the abdomen is not so easy, particularly when one bears in mind the frequency with which diffuse aneurism of the abdominal aorta has been mistaken for tumor. The important point is the character of the pulsation, which may be diffuse, even expansile, but rarely conveys to the hand that sense of force and strength communicated directly from an aneurism of the aorta or of one of the larger vessels. The bruit over the aneurism is usually louder, but it must be borne in mind that when the sac is very large and filled with masses of coagulum there may be no bruit.

Aneurisms Which do Not Pulsate.—There are two conditions in which an aneurism does not pulsate: (1) When a sac is obliterated with laminated fibrin. Sometimes met with in aneurism of the aorta, this is much more frequent in the popliteal and femoral vessels. In the latter regions it is a serious matter, as the leg may be amputated under the belief that the tumor is a sarcoma. Such an instance was seen in Montreal, in which there was a very large mass in the popliteal space which had neither pulsation nor bruit, but proved on dissection after amputation of the leg to be a completely obliterated aneurismal sac. A remarkable case is reported by Hulke¹ and the sequel is given by Baker² in his paper "On Aneurisms Which do Not Pulsate." A huge tumor, which proved at postmortem to be an aneurism, occupied the left side of the neck from the trachea to the vertebræ, passed behind the clavicle, filling the axilla, and passed through the superior aperture of the thorax into the left pleural cavity, occupying its upper third and compressing the lung. It sprang from the left subclavian artery. (2) The second condition in which an aneurism may not pulsate is when it ruptures into the neighboring tissues, forming a diffuse tumor. This may occur in the neck, as in the case reported by Hulke and Baker, but it is much more common in the abdomen. The tumor may be of enormous size and

¹ *Clinical Society's Trans.*, London, 1878, 11, 123.

² *St. Bartholomew's Hosp. Rep.*, 1879, 15, 75.

present slight, almost imperceptible pulsation. Sometimes no impulse whatever is to be felt, more particularly when the tumor extends rapidly in the flanks, forming a large solid mass. If the patient survives for weeks or months, the clots become firmer and the pulsation may diminish or even disappear entirely. But even very shortly after the rupture the pulsation may be readily overlooked in the intensity of the other symptoms. Many of them present the features of the acute abdomen, and there are a number of recent cases in which the patients have been operated upon, usually with the diagnosis of appendicitis, without the slightest suspicion that an aneurism was present.

Certain Special Points in Relation to Thoracic Aneurism.—Innominate or arch? The question is important with a view to surgical interference. The innominate is affected in many aneurisms of the arch, either uniformly dilated with it, or the orifice of the vessel is given off in the sac. The high position of the tumor, the presence of pulsation of the sterno-clavicular joint without pulsation in the second and third right interspaces, the extension of a definite tumor above the sternal notch, and above all the information to be obtained by the *x*-rays, are the important points. In young persons with aortic insufficiency there may be a prominent tumor above the clavicle, due to dynamic dilatation of the arch and innominate. In the following case a sac of the arch in a peculiar position led to a mistake in diagnosis: In 1879 there was in the Montreal General Hospital a man, aged thirty-eight years, with a strong pulsation above the right sterno-clavicular joint. On palpation the outlines of the tumor could be felt, with a smooth, rounded border just above and behind the joint. Vigorous lateral pulsation was felt with one finger in the sternal notch and the other at the outer border of the sternocleido-mastoid muscles. There was flatness behind the inner end of the right clavicle. A loud, systolic murmur was heard, but he had no aortic insufficiency. There was slight paralysis of the right cord. The question arose as to the possibility of cure by distal ligature, as the aneurism was thought to be of the innominate. He refused operation, and died of pneumonia about four months later. At the postmortem a dilated aortic arch was found, and just before the innominate was given off there was a small aneurism the size of a walnut, conical in shape, which passed up by the side of this vessel, occupying a position immediately behind the sternoclavicular articulation.

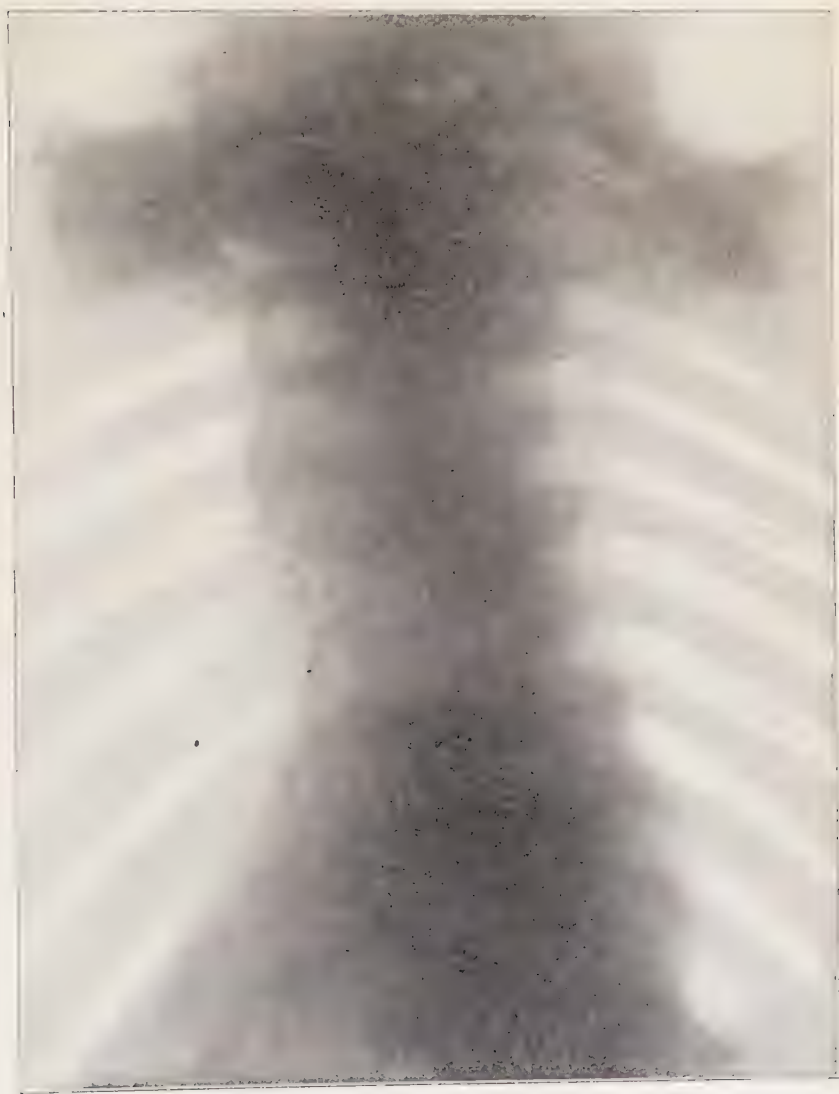
Roentgen-rays.—There is rarely difficulty in the diagnosis of the saccular aneurism, as the shadow pulsates and the rounded mass is readily differentiated. F. H. Baetjer, who had a very large experience with aneurism at the Johns Hopkins Hospital, classifies the positions as follows:

1. "Aneurism of the ascending portion of the aorta usually casts a shadow more to the right than to the left of the sternum, above the heart, and by localization would be found to be nearer the anterior than the posterior wall of the chest."
2. "Aneurism of the arch casts a shadow slightly to the left of the sternum, and this shadow extends well up into the neck, and by localization would be found nearer the anterior chest wall."
3. "Aneurism of the descending arch of the aorta casts a shadow to

the left of the sternum, and by localization would be found nearer the posterior than the anterior chest wall."

In dilatation, with the arch uniformly dilatated, a broad shadow extends along the sternum on both sides, and pulsation of the shadow may be

FIG. 102



Roentgenogram of an aneurism of the thoracic aorta.

seen and the shadow persists between pulsations. In the simple dynamic dilatation of the aorta, pulsation of the shadow is visible, but between the pulsations the shadow disappears, as the aorta contracts and its shadow lies within that cast by the sternum and the spine. In large

aneurisms the depression of the heart and its somewhat transverse position are usually well seen. It is particularly in the group of aneurisms without physical signs that the roentgen-ray examination is of the greatest possible value. One is greatly impressed with the accurate localization of the tumor in some of these latent cases. A woman, aged twenty-three years, was admitted cyanosed and with urgent dyspnoea. There was evidently tracheal compression. After she was relieved by venesection a most careful examination of the chest could detect but one physical sign—less air entered the lower lobe of the left lung than the corresponding lobe of the right lung. The roentgen-ray examination showed a small aneurism of the transverse arch; the position corresponded accurately with that as determined postmortem. Several of the latent cases presented only persistent pain. In skilful hands there is rarely much confusion between aneurism and tumor. Williams, the pioneer in radioscopic work in internal medicine in America, very fully sums up the position in the following words: "To make a definite diagnosis of aneurism by the usual physical examination we may be obliged to wait for the development of marked signs, and this delays treatment. On the other hand, if the physician begins treatment because the signs are suspicious, he runs the risk of subjecting his patient to unnecessary regimen. The advantages of roentgen-ray examination when compared with the usual physical examination are evident. A definite diagnosis can be made in most cases before there are physical signs. Treatment can, therefore, be begun at an earlier and more hopeful stage, can be planned more intelligently as the knowledge of the position and extent of the aneurism is more accurate, and its results can be better estimated because we can more accurately measure any change in size."

Prognosis.—In aneurism of the aorta the outlook is always grave, and yet a number of cases recover. The mode of cure has been spoken of. Lebert estimated that the period of the evolution of an aneurism was from six months to four years. In a great majority of all cases the fatal result occurs within two years from the onset of the symptoms. The most favorable is the saccular form projecting anteriorly or to the right, but it is not always easy to determine the exact shape, although now with the roentgen-rays one can often get a very good idea of the form. Once an aortic aneurism is healed, the individual may live for many years. Under Dissecting Aneurism the case of a soldier who was invalidated for aneurism after the Crimean War, in 1855, and who lived until 1881, was mentioned. Among favoring elements in the prognosis are: (1) Position and form of the sac. Moderate-sized, saccular aneurisms of the ascending arch, of the descending part, and of the abdominal aorta are more frequently seen obliterated than those springing from the transverse arch. (2) Early diagnosis and treatment. In the case of a young man who has had syphilis, specific treatment thoroughly carried out, in combination with absolute rest, gives at least a chance of cure. (3) In a few instances the sac projecting anteriorly has been permanently occluded as a result of operation. The San Francisco case operated upon by Rosenstern lived for many years. Even after a sac has perforated the chest wall, life may be prolonged. Jamieson reported the case of a man aged thirty-two years, who lived and worked for

twelve years with an aneurism projecting through the chest wall. There are deceptive features in thoracic aneurism which must be taken into account in the prognosis. The pulsating tumor may diminish, may even disappear, and yet the sac may increase in another direction. In a case of this kind, the patient had been given a strict Tufnell treatment, and had taken iodide in large doses. The pulsation anteriorly had lessened remarkably, and it was thought that the aneurism was healing, but he died suddenly of rupture into the pleura, into which, it was found at post-mortem, the sac had extended.

Death takes place usually from the rupture of the sac, sometimes from sudden paralysis of the heart, rarely from the effects of pressure or from gradual asthenia.

Treatment.—Necessarily in great part symptomatic, only in a few cases is a cure effected. In a case of thoracic or abdominal aneurism seen early the following plan of treatment may be carried out:

1. *Rest.*—By diminishing the vigor of the heart's action, and possibly by diminishing the volume of the sac, there is often an extraordinary relief to the cough, the shortness of breath, and the pain. The rest should be complete, the patient remaining for from six to twelve weeks in the recumbent posture and making as few movements as possible. It is not an easy treatment to carry out. If the aneurism is large and has already eroded the chest wall, it is hardly worth while to insist upon prolonged rest. Between the recumbent posture and the erect with exercise the reduction of the number of pulsations per minute in the sac may be from twenty-five to thirty, so that in the course of the day there is a considerable saving of the strain upon its walls.

2. *Diet.*—The intake of solids and liquids may be reduced to a minimum. Tufnell's diet¹ is as follows: "For breakfast, two ounces of bread and butter and two ounces of milk or tea; dinner, three ounces of mutton, three ounces of potatoes or bread, and four ounces of claret; supper, two ounces of bread and butter and two ounces of tea; total *per diem*, ten ounces of solid food and eight ounces of fluid, and no more." Only in early cases is it worth while to put the patient to the serious inconvenience of this diet.

3. To aid in the reduction of the blood pressure, and to increase the tendency to coagulation in the sac, small bleedings may be practised, five or six at intervals of a week, taking six to ten ounces of blood. This triple combination of rest, low diet, and bleeding is the Valsalva method, which was used with success by Albertini and other Italian physicians in the eighteenth century. Morgagni gives it succinctly: "When as much blood as was requisite was withdrawn (by repeated small bleedings), he (Valsalva) ordered a progressive diminution of food and drink until the quantity was reduced to a determined weight of aliment and water. Having so enfeebled the patient that he could scarcely raise his hand from bed, on which he was ordered to lie from the beginning, the quantity of aliment was cautiously increased." Morgagni remarks: "There are many persons to whom Valsalva's method of cure may appear more intolerable than the aneurism itself, especially at the

¹ *Med. Chir. Trans.*, London, 1874, 57, 83.

only time when any treatment could avail. The inconvenience of the disease at that period is but slight and the danger is not imminent, etc."

4. *Mercury and Arsphenamine*.—There is no doubt in the minds of the modern students of syphilis, that courses of mercury and arsphenamine should be instituted in every case of aortic syphilis, even when aneurism has resulted. Schottmüller¹ believes that "since the advent of specific arsphenamine treatment, syphilitic aortitis should always be grouped under curable diseases." The junior writer can only express his own belief in the harmlessness of the combined method of treatment and in its apparent beneficial effect upon the course of syphilitic aortitis with aortic valve disease and even in the still more advanced stage when an aneurism has developed. Small doses of neo-arsphenamine are given at five or seven day intervals until at least 5 or 6 gm. have been administered in the course of three months. At the same time, mercury should be given to a point short of saturation, by inunction, hypodermically or intravenously in the form of calomel or salicylate of mercury. After a three months' interval a second course of this intensive treatment should be instituted, unless the patient can return for a monthly combined treatment over a three years' period.

5. *Iodide of Potassium*.—The value of this drug in aortic aneurism is undoubted. Formerly the favorable results were attributed to condensation of the sac by its action on the fibrous tissues and to the promotion of coagulation. A more rational view is that the luetic mesarteritis is directly influenced by it. It is remarkable with what promptness the pain is relieved in the syphilitic cases. Formerly we gave enormous doses, up to 200 and more grains three times a day, but moderate doses are just as effective, and it is rarely necessary to give more than 25 to 30 gr. (1.5 to 2 gm.) three times a day.

6. *Measures to Allay Pain*.—The iodide of potassium often gives relief. Local applications—belladonna plasters, an ice-bag, a hot poultice, or a hot-water bottle—are helpful, but in the majority of cases, when the pain is due to pressure, morphine must be given. And in such a desperate malady it is well to give it early and freely.

7. *Additional measures employed to increase the coagulation of the blood*. To assist the low diet and rest and iodide of potassium in promoting the coagulability of the blood, calcium lactate may be given in from 15 to 20 gr. (1 to 1.3 gm.) doses three times a day.

Not in every case of thoracic or abdominal aneurism should a cure be attempted. A majority of the patients come under observation at a period when symptomatic treatment is alone possible. In what class of cases may a cure be expected? In the young syphilitic subject under thirty, in whom the diagnosis is made early, in cases in which the fluoroscope shows a small and sacculated aneurism, and in elderly persons, in whom, as postmortem experience teaches, the sac may spontaneously heal. When the sac is large, or if the fluoroscope shows a diffuse dilatation of the arch, it is best to allow the patient to continue his occupation, unless it is too arduous, and treat the symptoms as they rise.

What is to be done to relieve the frightful pressure *dyspnœa*? Patients are not infrequently brought to hospital cyanosed, gasping for breath

¹ *Am. Jour. Syph.*, 1925, 9, 1.

and literally choking to death. As already stated, it is not always easy at first to make a diagnosis, but it is well to remember that in 9 out of 10 of such cases in adult males aneurism is the cause. Venesection from one or both arms to 25 or 30 ounces may give prompt relief. The removal of much smaller amounts may be effectual. It may be repeated several times in the course of a week. There are very few conditions in which free bleeding is so helpful. Morphine hypodermically should be given, unless there is an extreme degree of pulmonary infiltration, as shown by fine bubbling rales. In any case, if the patient is *in extremis* and suffering, it should be given. In the paroxysmal dyspnoea suggesting spasm of the larynx, due to irritation of the recurrent laryngeal nerves, the inhalation of chloroform may be tried; even if not immediately relieved, the comfort to the sufferer is very great. Should tracheotomy ever be performed in these cases? Theoretically, of course, with an aneurism or a tumor garroting the trachea at the bifurcation, it is useless, and yet it is often impossible to resist in the case of a poor fellow admitted choking and in a dying state. The senior writer saw it done in a good many cases, never with permanent benefit, occasionally with temporary relief. In one case the woman's suffering was so frightful that after a preliminary tracheotomy Dr. Halsted attempted to reach the seat of compression by resecting the upper portion of the sternum, on the chance of giving freedom in this way and possibly of placing one of his rings about the aorta above the sac, the position of which could be accurately defined with the fluoroscope. The patient died on the table in a paroxysm.

Surgical Treatment of Internal Aneurism.—*Ligation of the aorta* has been done ten or twelve times for aneurism of the abdominal aorta, always with fatal result.¹ *Digital compression* has been tried in many cases. William Murray, of Newcastle-on-Tyne, cured a man aged twenty-six years, who had a pulsating tumor to the left of, and above the umbilicus. Between the sac and the free border of the rib there was room enough to permit one part of a tourniquet to press on the spine and control the pulsation. The patient was put under chloroform for two hours, during which time the pulsation was arrested. On removal of the pressure there was no effect. Three days later the pressure was again applied under anesthesia of five hours' duration. In the last hour the pulsation was no longer evident when the tourniquet was released, the extremities were cold, and the femorals could not be felt. The patient got perfectly well and lived six years, when another aneurism occurred at the celiac axis.² A number of successful cases have been reported. When by digital compressions or a tourniquet the pulsation in the sac may be obliterated, this is the safest method. But it is not always satisfactory, and death has followed from peritonitis, obstruction of the bowels, and reduction of the pancreas to a pulp.

Insertion of Foreign Bodies in the Sac.—In 1864, C. H. Moore, of the Middlesex Hospital, attempted the cure of aneurism by the introduction of wire into the sac, believing that by it coagulation of the

¹ *Phila. Med. Jour.*, 1900, 5, 470.

² *Medico-Chirurgical Society's Transactions*, 1864, 47, 187; *Inductive Method in Medicine*, Murray, 1891, p. 120.

blood would be favored. He put 78 feet of fine wire into the sac of a thoracic aneurism. Death occurred on the fifth day. Many other substances have been used, catgut, horsehair, Florence silk, etc. It has not been a very successful method, though Colt's modification of the "wire-wisp," as described by Darcy Power,¹ has resulted in a few cures and the relief of pain in some other patients.

Electrolysis.—Corradi recommended the passage of an electrical current through the wire inserted into the sac, and this Moore-Corradi method is the one most frequently used. The operation may be performed with safety in suitable cases. Of 23 cases treated in this way, 17 thoracic and 6 abdominal, 4 were cured. Three cases were improved. In 10 cases death was probably hastened. Of the series of cases of aneurism of the abdominal artery, 7 were treated by the Moore-Corradi method, 2 were improved, and 1 was alive three and a half years after the operation. The sacculated tumor with small orifice is best adapted for this, and with the improved facility afforded by the roentgen-rays in determining the position and shape of the aneurism the chief difficulty will be overcome in the selection of suitable cases.

Needling the Sac.—Macewen introduced the practice of needling the inner lining of the aneurism with a view of promoting thrombus formation. It has been successful in a few cases. The practice of injecting irritating liquids into the sac has been given up.

For the statistics of the surgical treatment of the important recent series of cases of arteriovenous aneurism the reader is referred to W. F. Stephenson's *Report on the Surgical Cases in the South African War*, London, 1905, p. 223, and to the paper by Saigo in the *Deutsche Zeitschrift f. Chirurgie*, Band xxxv, on traumatic aneurism in the Russo-Japanese War. The results of the more modern surgical treatment of gunshot injuries sustained in the recent World War are given by Makins.²

Still more encouraging results are reported by M. R. Reid³ in a series of papers in 1925: His conclusions are in brief "When it is possible to wait, arterio-venous aneurisms should not be operated earlier than from three to six months after the injury. In this time healing may occur and an abundant collateral circulation will develop. In general extirpation of the involved vessels yields the best results. . . when an arterio-venous aneurism has been present for any length of time; whereas in very early cases restoration of both vessels or of the artery, when possible, may be desirable. In all operations on large arteries an effort should be made to establish a normal vascular equilibrium in the part supplied by those vessels. This probably means that when a large artery is tied the accompanying vein should also be ligated."

Reid urges surgical treatment for the majority of cases as "a fistula between large vessels may lead to grave cardiac disturbances or even sudden death." Leriche, Holman and others have reported cases in which a dilated or hypertrophied heart returned to its normal condition following the cure of the fistula.

¹ *Brit. Jour. Surg.*, 1921-1922, 9, 27.

² *Ibid.*, 1915, 3, 353.

³ *Arch. Surg.*, 1925, 10, 601, 996, 1925, 11, 25, 237.

CHAPTER XXIV

THROMBOSIS, EMBOLISM, AND PHLEBITIS

By GEORGE BLUMER, M.D.

THROMBOSIS

THROMBOSIS may be defined as "the formation of a solid mass or plug in the living heart or vessels from constituents of the blood" (Welch). The term thrombus is applied to the plug so formed.

Etiology.—Leaving aside the occasional occurrence of thrombosis as a direct result of trauma, the chief factors concerned in the production of spontaneous thrombi may be grouped as follows: (1) *Mechanical factors*, i. e., conditions altering the blood flow, (2) changes in the *blood plasma* affecting the coagulability of the blood, (3) changes in the *formed elements* of the blood, particularly the platelets and (4) changes in the *walls of the vessels*.

1. Aschoff¹ has pointed out that, at any rate in times of peace, the *mechanical factor* is probably the most potent. Both clinical and pathological evidence makes clear that the great majority of thrombi, those in the immediate neighborhood of infectious processes excepted, occur in those parts of the circulatory system where the greatest opportunity for slowing of the blood current exists. The frequent occurrence of thrombosis in the auricular appendages of the heart, particularly when abnormalities of the heart beat or general myocardial weakness preëxist, has long been known. Equally obvious is the fact that the process in the venous system is not of haphazard distribution but selects certain vessels in which, for various reasons, slowing of the blood current is apt to occur. The pelvic, splenic and prostatic veins, among those of the interior of the body, and the femoral and saphenous veins of the extremities may be cited to illustrate this point. The relative infrequency of thrombosis in arteries is added evidence of the importance of slowing of the blood stream.

The *histological structure* of spontaneous thrombi strongly supports the view that they occur, almost without exception, in association with a slowing or eddying of the blood current. Only under such physical conditions as are associated with retardation or eddy formation could we have the orderly laying down of platelets with the secondary leukocytic deposition which characterizes the first step in thrombus formation. The red thrombus which, in many instances, forms the greater part of the finished clot does not result until the circulation has been brought to a standstill by an obstructing white thrombus. This part of the clot is made up of the normal constituents of the blood in their usual proportions with a certain amount of fibrin where the red and white portions of the clot adjoin one another.

¹ *Lectures on Pathology*, New York, Hoeber, 1924.

2. A discussion of the part played in thrombosis by changes in the *blood plasma* brings up the moot question of the physiology of blood coagulation. It is now quite generally conceded that coagulation does not play as important a part in thrombosis as was once assigned to it. It is to be noted from the brief description of the histology of thrombi in the preceding paragraph that the formation of fibrin is not an outstanding feature. The primary process is an agglutination or conglutination of blood platelets the exact cause of which is still in doubt. It is possible that changes in the plasma may play a part in this but there is no definite proof that such is the case, though for a time considerable attention was paid to the possible role of substances (agglutinins) causing adhesions of platelets.

3. Evidence regarding the presence of changes in the *morphological elements* of the blood in thrombosis is scant and unsatisfactory. Inasmuch as the initial stage in spontaneous thrombosis is agglutination of the blood platelets it has sometimes been assumed that changes in these structures favor thrombosis but convincing proof of this is lacking.

4. In the case of thrombosis associated with local *infectious processes* there is little doubt that alterations in the *vessel walls* play an important part in the process. In thrombi not associated with local infection or even where thrombosis occurs at a distance from local infectious processes there is little evidence that such changes are present. Indeed such thrombi usually occur in the locations mentioned under "mechanical factors" and these latter probably play the most important role in the thrombus formation. There is little evidence to support the view stressed mainly by French writers that thrombosis is always an infectious process.

Racial and family peculiarities exist. The strong tendency of the Jewish race to thrombo-angiitis has been well demonstrated. Aside from this racial tendency to thrombosis, there are undoubtedly certain families in which a similar tendency exists. Such families may be described as thrombophilic in contrast to hemophilic families in which a tendency to bleed is a pronounced feature. In time it may be shown that in such families changes exist in the normal coagulability or in the agglutinability of the blood.

Etiological Relationship of Various Diseases to Thrombosis.—The occurrence of thrombosis with certain diseases is well recognized and a knowledge of its disease associations is therefore desirable.

Typhoid Fever.—Cardiac and arterial thrombi are rare in typhoid fever. Arterial thrombosis occurs in about 0.35 per cent. of all cases, according to Thayer. The lesion generally attacks the leg and, when complete, usually results in gangrene. In some cases the thrombus does not completely occlude the vessel and perfect recovery occurs. In contrast to venous thrombosis in typhoid, the two sides are equally affected. The visceral arteries, especially the middle cerebral, are not infrequently involved. The complication usually occurs during the febrile period.

Venous thrombosis occurs, according to Thayer, in two and one-half per cent. of all cases of typhoid fever. In the great majority of instances the veins of the lower extremity are involved and the left side much more frequently than the right. The popliteal, iliac, and calf veins are stated

to be involved only one-fourth as frequently as the femoral veins. This statement is open to doubt, as many femoral thromboses begin in involvement of the deeper veins, especially those of the calf.

Pneumonia.—*Cardiac* and *arterial* thrombosis is rare in pneumonia. Most of the cardiac thrombi which are described in the literature as occurring in this disease are postmortem, the mistake being due to the unusually firm postmortem clots found in this disease. Thrombosis of the peripheral arteries is much less common than embolism and is usually associated with great feebleness of the circulation. The occurrence of *venous* thrombosis is probably less infrequent than the literature would indicate. The small number of cases which Steiner was able to collect probably gives an entirely false impression of the frequency of the complication. In the past ten years the writer has observed a good many cases. The thrombosis usually involves the lower extremities, especially the femoral vein, the left side being much more frequently attacked than the right.

Influenza.—*Cardiac* thrombi of a marantic nature have occasionally been reported and a few instances of globular thrombi are on record. Thrombosis in association with an influenzal endocarditis has been reported a number of times in recent years. *Arterial* thrombosis, while more common in influenza than in most of the infectious diseases, is comparatively rare. According to the German statistics, it occurs in only 0.005 per cent. of all cases. The vessels of the lower extremities are attacked in the great majority of instances. The figures, both of Welch and of the German Committee, show that the popliteal artery is most frequently involved; next, the femoral; and less frequently, the iliac, axillary, and brachial. The cerebral and occasionally the pulmonary arteries are thrombosed in this disease.

Venous thrombosis is comparatively frequent, usually occurring either late in the attack or during convalescence. The veins of the lower extremities are usually involved, though the brachial and axillary seem to be more frequently thrombosed than in other infections. The severity of the disease seems to have little bearing upon the likelihood of thrombosis. There are too few cases on record to satisfactorily substantiate Leichtenstern's view that venous thrombosis in influenza is more apt to lead to gangrene than venous thrombosis associated with other diseases.

Postoperative Thrombosis.—The association of thrombosis with operative procedures, particularly with abdominal operations, has been a subject of much comment. Beckman's figures from the Mayo Clinic, based upon 3657 consecutive cases, show 0.0046 per cent. with thrombosis. Certain abdominal operations seem more likely to give rise to this complication than others, and operations for splenectomy, for uterine myomata and appendicitis seem especially prone to be followed by thrombosis. In many instances it occurs in cases which are apparently entirely free from sepsis. The condition usually involves the veins of the lower extremities, especially the left femoral vein, and this entirely independent of the site of incision and operation. Much discussion regarding the etiology of this form of thrombosis has resulted in a wide diversity of opinion. Some writers, as Clark, incline to place the chief blame on mechanical conditions, such as trauma to small vessels during operation.

They believe that the involvement of the femoral is secondary to a spread from these smaller tributaries. While pathological evidence shows that this may occur it is the exception rather than the rule. Other writers hold that phlebitis due to an attenuated sepsis is at the bottom of most cases and this is substantiated in some cases, at any rate, both by the febrile course of the complication and by the fact that bacteria have occasionally been isolated from such thrombi. Their frequent occurrence in connection with the removal of the uterus and ovaries has led to the hypothesis that the internal secretions of the female sexual organs exert some influence on the process but there are no solid grounds for such a belief. There is evidence which tends to show that the complication is less frequent in patients who are allowed to sit up and get out of bed at a comparatively early period after operations. The subject is still unsettled and it is probable that different factors are of importance in different cases.

Rheumatic Fever.—All forms of thrombosis are exceedingly rare in this disease. Cardiac thrombosis, aside from that occurring with a complicating endocarditis and arterial thrombosis, is almost unknown. Venous thrombosis is rare and when present is usually in the veins of the lower extremities and associated with a definite phlebitis.

Tuberculosis.—*Cardiac* thrombi occur, according to Ruge and Hierokles, in but two-tenths of 1 per cent. of patients dying of pulmonary tuberculosis. *Arterial* thrombi are also very uncommon, though occasionally small parietal thrombi form on the intima of the vessel in acute miliary tuberculosis. *Venous* thrombosis occurs in something over 1 per cent. of all patients with chronic pulmonary tuberculosis and may be symptomatically latent. The process may occur early but is most common during the terminal stages. Women are said to be more subject to it but the figures are too small to prove this statement satisfactorily. As in other forms of venous thrombosis, the peripheral veins of the lower extremities are most frequently involved, though the veins of the internal organs and of the arms are occasionally affected. The enfeebled circulation which accompanies the terminal stages of chronic tuberculosis and the frequency of terminal infections are probably the important factors.

Gonorrhœa.—All forms of thrombosis are rare in gonorrhœa though venous thrombosis is much more common than the cardiac or arterial forms. When it occurs, it affects men in over two-thirds of the cases. It generally appears in the subacute stages of a first attack and involves the veins of the lower extremities, particularly the internal saphenous. The cerebral sinuses and veins of the upper extremities are occasionally involved, as are the veins of the genitalia. Gonorrhœal arthritis is a not infrequent accompaniment of thrombosis, suggesting that the thrombus formation is a manifestation of a gonococcus septicemia.

Syphilis.—*Cardiac* and *arterial* thrombosis are both very rare during the course of syphilis, if we except the thrombosis occurring in connection with syphilitic aortitis accompanied by aneurism. Of the peripheral vessels, the veins are the ones most frequently attacked by the luetic infection, and thrombosis usually occurs in connection with phlebitis. The process may occur at any time but is most common in the secondary

stage. It is much more common in males than in females and seems most likely to occur in those whose occupation keeps them on their feet. The veins of the lower extremities are especially apt to be involved, and, as in gonorrhœa, the internal saphenous vein is more frequently involved than any other. Multiplicity of involvement is common, as are successive exacerbations of the process in the same vein. The symptoms come on insidiously in many instances. There is a rare form of the disease known as syphilitic erythema nodosum or nodular thrombo-phlebitis, in which red or violet nodosities resembling those of erythema nodosum appear along the course of the veins, usually those of the lower extremities or the corpus cavernosum.

Chlorosis.—Cardiac and arterial thrombosis in chlorosis is very unusual. Venous thrombosis, on the other hand, is a relatively common complication. Leichtenstern estimates that thrombosis occurs in about 1 per cent. of chlorotics. His figures show that the veins of the lower extremities are involved almost exclusively, if the peripheral vessels only are taken into account. Thrombosis of the cerebral sinuses is reported hardly less frequently, however, but the published figures give an entirely erroneous impression regarding the frequency of sinus thrombosis, which is rare. In the lower extremities the smaller veins, especially the calf veins, are frequently involved, and for this reason the process is much more likely to be overlooked than when the femoral or internal saphenous are occluded. The left leg is more frequently affected than the right, and bilateral involvement is exceedingly common. The percentage of emboli resulting from peripheral thrombi in chlorosis is very high compared to thrombosis associated with other conditions. Welch states that there is embolism in 25 per cent. of the cases. This renders the prognosis of chlorotic thrombosis graver than that of any other form with the exception of puerperal thrombosis.

Miscellaneous Parasitic Diseases and in Cachexia.—Thrombosis has occasionally been described in a variety of other infections. In dysentery both arterial and venous thrombosis is occasionally met with, also in chronic diarrhœa, especially in feeble infants and old people. In Asiatic cholera, diphtheria, erysipelas, chronic suppuration, plague, measles, peritonitis, dental caries, nephritis, and scarlet fever, occasional instances of thrombosis are reported. Typhus fever is the infectious disease most commonly associated with arterial thrombosis but this rarely occurs in the attenuated form in this country. Thrombosis in malaria is rare, many of the cases reported being doubtful. In the cachexia associated with malignant neoplasms and in anemias of the severer grades, thrombosis is not unusual. Where predisposition exists, thrombosis may even result from the pressure of the cuff used in determining blood-pressure. The cachectic thromboses are associated with a variety of causes, especially degenerative changes in the bloodvessels, enfeeblement of the circulation, and terminal infections.

Cardiac Disease.—The thrombi which occur in the heart itself are practically never recognized clinically, but arterial thrombosis may occur, especially associated with endocarditis, and is not difficult of recognition. In decompensation, arterial thrombosis is hardly ever en-

countered, while peripheral venous thrombosis is a not infrequent complication. The peripheral *venous* thrombosis of decompensated heart disease differs mainly from that in other conditions in the great preponderance of the involvement of the vessels of the upper extremities. The complication attacks males more often than females and occurs most frequently in patients with mitral valve disease between the ages of fifteen and thirty. It is common for more than one vessel to be involved, and the most usual combination is a continuous thrombosis of the innominate vein, the internal and external jugular veins, and the subclavian and axillary veins. The left side is much more frequently attacked than the right, partly because there is frequently a developmental error on that side near the junction of the internal jugular and subclavians, and partly because the pressure of the dilated left auricle comes into play. There is also an unusual opportunity for the formation of eddies in the jugular bulb. As these patients are generally in the last stages of decompensation, and frequently have also a terminal infection, the outcome is usually fatal. However, I have seen 2 cases in which compensation was reestablished after the development of a venous thrombosis.

Gout.—Two types of thrombo-phlebitis have been described in connection with gout. In one, there is no question of the relationship as the complication occurs during the attack, probably as the result of the extension of the inflammatory process, the veins in the neighborhood of the inflamed joint becoming thrombosed. The second type was stated by Paget to occur in persons of marked gouty constitution or with gouty inheritance. Inasmuch as similar cases have been described without any history of gout, we may be pardoned if we are skeptical concerning the gouty nature of many of them, especially when we remember the loose way in which the term gout is used by English writers. It is probably better to describe these cases under the heading of *idiopathic recurrent thrombo-phlebitis* or *phlebitis migrans*. There is a strong hereditary tendency in many of these cases, which resemble, in their tendency to recurring attacks, certain cases of syphilitic phlebitis and the condition of thrombo-angiitis obliterans. The disease usually attacks the superficial veins of the lower limbs, involving short segments of the vessels, recurring frequently without obvious cause, and producing comparatively little local or general reaction. The left side is more frequently involved than the right, and the leg more frequently than the arm. There is disagreement regarding the danger of secondary embolism.

Primary Infective Thrombosis.—There are a few reported cases of patients presenting the clinical picture of general sepsis accompanied by widespread thrombosis, both in the veins and arteries, but usually predominating in one group of vessels. The most striking clinical feature in some of these patients is the absence of symptoms and physical signs at all comparable in severity to the extent of the vascular lesions. In the patients of Dowse and Osler, this latency of symptoms was not very marked as the peripheral vessels were the ones mainly involved. In the very remarkable cases of Eichhorst, the lack of marked symptoms referable to the internal organs, in spite of widespread thrombosis of their vessels, was a striking feature. Eichhorst's conception of the condition is that it is

a sepsis in which, as the result of bacterial infection through the vasa vasorum, localized areas of arteritis with thrombus formation are produced. It is possible, however, that in some instances the infection occurs through the intima by way of the circulating blood.

Special Pathology.—Structure of Thrombi.—In the common varieties of thrombi the plug is constituted of the formed elements of the blood, the red and white corpuscles, and the platelets, plus fibrin. The main factor which decides the appearance and structure of such thrombi is the physical condition of the blood stream at the time the thrombosis occurs. If the process involves stagnating blood, a red or cruor thrombus occurs. If the blood is still circulating, a white thrombus results. Mixed thrombi occur when, during the formation of a white thrombus, the circulation is markedly impeded or stopped, so that portions of the plug are composed of stagnating or almost stagnating blood, or they may occur from fissuring of a white thrombus with a formation of red thrombi in the fissures.

Thrombi are apt to be confounded with postmortem clots, the distinction between the two being, however, usually not very difficult. The postmortem clot is common in the cavities of the right side of the heart, in the cerebral sinuses, and in the veins. It may be entirely red, or, what is common in the heart especially, mixed red and yellow, the yellow portion often having a striking resemblance to chicken fat. In the heart such clots often penetrate between the columnæ carneæ, giving a false impression of being adherent, but are easily detached and with very little experience can be distinguished from true mixed or white thrombi which are usually so firmly adherent that they cannot be removed without tearing. In the vessels also, postmortem clots which are partly yellow and partly red may be formed and may be taken for mixed thrombi. In this instance the red portion of the clot is the dependent portion, and here again the clot, as distinguished from the true thrombus, is easily detached from the vessel wall. The grayish color and opaque appearance of the white thrombus is usually quite different from the yellowish color and semi-transparent appearance of the postmortem clot. The consistency of the two is different, the postmortem clot being elastic and homogeneous, the thrombus granular and rather friable. The peculiar ridging of the surface of certain thrombi is never seen in postmortem clots. These remarks refer particularly to the white or mixed thrombi. Red thrombi when recently formed may be much more difficult to distinguish from postmortem clots. Usually in red thrombi the deposition somewhere on the surface of a white film composed of leukocytes, platelets, and fibrin serves as a point of differentiation. In older red thrombi the marked adherence to the heart or vessel wall and the granular consistency render differentiation easy.

Microscopically red and white thrombi differ considerably in structure. Red thrombi are composed of the formed elements of the blood, in approximately their normal proportions, traversed by fine strands of fibrin. White thrombi are made up of a framework of granular material composed of fused blood platelets, in the meshes of which are red and white corpuscles and fibrin in proportions which vary according to the rapidity of the blood stream at the point of thrombus formation. Leukocytes are

usually present in good numbers, especially along the edges of the platelet network, and fibrin threads occur mainly among the leukocytes. Red corpuscles are not numerous if the circulation was rapid when the thrombus formed, but may be present in large numbers if the circulation was feeble. It is on the surface of white or mixed thrombi that the transverse ridges, described especially by Zahn, may be seen. They run at right angles to the long axis of the vessel, lie roughly parallel to one another, and may be united by fine oblique striations. The appearance is due to a physical action of the circulating blood upon the viscous surface of the thrombus similar to that produced on the sand of river banks or the seashore by the waves.

Method of Formation of Thrombi.¹—Different ideas have been held at various times as to the nature of thrombus formation. Briefly stated, the two main views have been: (1) That it is merely a process of coagulation. (2) That the essential process is an agglutination of the blood platelets with which coagulation is associated as a secondary process. The idea that thrombosis is coagulation pure and simple has now been abandoned by most pathologists; at any rate, so far as the formation of the more common white or mixed thrombi is concerned. The generally accepted view as to the formation of such thrombi based upon experimental work and the study of human lesions, indicates that the first step in the thrombus formation is the accumulation of blood platelets at the point where the lesion occurs. The observations of Pratt show that red blood corpuscles are also present in the early stages. This is followed by the transformation of the platelets into a sticky mass (viscous metamorphosis) which causes them to adhere to one another and to the vessel wall. Later polynuclear leukocytes accumulate in the interstices of the mass, and fibrin appears. Red corpuscles are present in numbers varying inversely to the rapidity of the blood current at the site of thrombus formation. The latter part of the process is believed to involve the ordinary changes which accompany coagulation.

The manner of formation of the agglutination thrombi composed of red blood corpuscles, which occur in connection with certain infections and intoxications, has been described by Flexner. The red corpuscles fuse as a result of the action of the poison into a dark, soft, conglutinated clot, the fluid portions of the blood being laked in appearance. Sections of experimental clots show agglutination of some of the red blood corpuscles, others appearing as shadows. Fibrin is not present in these experimental clots. In man such agglutination thrombi are made up of conglutinated masses of red cells with a few leukocytes, usually along the walls of the vessels, and but little fibrin. There seems no doubt that in the later stages of such thrombi, transformation of the fused mass occurs, and the appearance is then that of the so-called hyaline thrombi.

Accepting Welch's definition of a thrombus as a plug formed during life from constituents of the blood, we must recognize two other varieties of thrombi which occur occasionally, viz., leukocyte thrombi and fibrin thrombi. Welch expresses the opinion that the formation of ordi-

¹ L. Loeb, *Virchow's Archiv.*, 1906, vol. 185.

nary white thrombi from leukocytes, if it occurs, must be a rare event. In connection with local inflammatory lesions, however, a plugging of the regional vessels with leukocytes is not uncommon. Thrombi composed of fibrin from the beginning, as distinguished from old thrombi which have undergone fibrinous transformation, occur merely in small vessels and have no clinical interest; they at times undergo transformation into hyaline material, constituting one variety of hyaline thrombi.

Growth in Thrombi.—Most vascular thrombi when they originate lie along one side of the vessel, constituting mural or parietal thrombi. In the cavities of the heart parietal thrombi are the rule, and are usually in the form of rounded or flattened masses projecting into one of the heart cavities. The auricular appendage may be completely filled with a thrombus mass, and a polypoid continuation into the auricular cavity is not uncommon. When, as occasionally happens, a thrombus becomes free in the auricle it may assume a globular form, and then constitutes a so-called ball thrombus. The vascular thrombus does not as a rule remain parietal, but ultimately fills the vessel, occluding the lumen (occluding or obstructing thrombus). It then usually extends, commonly in the direction of the blood stream, occasionally in an opposite direction. As a rule the extension ceases when the first branch of the vessel capable of reëstablishing the circulation is encountered; but this is not always the case, and thrombi may extend into the branches or may be continued on one wall of the vessel beyond the branch as parietal thrombi. When prolongation of the thrombus occurs, the extended portion is often much less adherent to the vessel wall than the original thrombus, and the terminal end of the growing thrombus is usually cone-shaped and entirely free in the blood stream. A marked extension of the thrombus seems more apt to occur in veins without valves. Infective thrombi are more liable to extend widely than aseptic ones.

Secondary Changes in Thrombi.—The most important of these is the process of organization which is essentially the same in all forms of thrombi. The active participants in the organization are the endothelial cells lining the vessel or heart, the connective-tissue cells of the cardiac or vascular wall, and the vasa vasorum. The process is often preceded and usually accompanied by degenerative changes in the thrombus, transformation of the platelet masses into a granular material, degeneration of the leukocytes, decolorization and disintegration of the red corpuscles with hematin formation, increase in and coarsening of the fibrin strands, and more or less retraction and fissuring of the thrombus mass. In the actual process of organization the thrombus plays a passive part, acting for the time as a temporary scaffolding for the advancing vessels and connective-tissue cells, ultimately being removed, mainly by phagocytosis. The process consists in the vascularization of the clot by newly formed vessels which are pushed in as sprouting processes from the preëxisting vasa vasorum, and which are accompanied by newly formed connective-tissue cells originating either from those preëxisting in the vessel wall or from the actively dividing endothelial cells of the intima. These proliferated intimal cells coat over the surface of the thrombus which is exposed to the blood stream, penetrating into the crevices and crannies

formed by the retraction or fissuring of the clot. According to some observers newly formed vessels may also originate from the endothelial cells. The process results in replacing the thrombus by connective tissue, at first vascular and made up of an embryonic type of cell, later becoming fibrous and poor in vessels like cicatricial tissue. The ultimate result so far as the vessel is concerned may be a complete plugging with transformation of the thrombosed area into a fibrous cord, or more commonly a partial or even complete restoration of the circulation, either as a result of retraction of the organized thrombus or the formation through it of a series of blood channels. Occasionally a complete disappearance of the organized thrombus occurs, or it is represented by a few fine, thread-like adhesions which in no way interfere with the circulation.

The rapidity with which organization of the thrombus takes place is a matter of considerable importance, as the danger from secondary embolism gradually decreases as organization progresses. There are, of course, great individual differences in the capability of repair. In favorable cases organization may be well under way within a week. Certain factors may delay organization, such as infection, and disease of the heart or vessel wall. The importance of the latter factor can be realized when it is remembered that the process of organization proceeds from the tissues of the cardiac or vascular parietes. Under certain circumstances salts of lime are deposited in thrombi, more especially in venous thrombi. Rarely the calcified thrombus in its original form is transformed into a stony cylinder; more commonly calcified thrombi are in the form of spherical calcific nodules with smooth surfaces lying in the vein or artery almost free from attachment, and constituting phleboliths or arterioliths. The vein-stones are much the more common, look like small seed pearls, and are most often met with in varicose veins, in the veins of the spleen, and in the smaller pelvic veins, especially those about the base of the bladder.

Secondary degenerative changes in thrombi in the form of liquefaction or softening are of great practical importance on account of the increased danger from secondary embolism associated with them. Two forms of softening are generally recognized, the bland and the infective, the latter form being again subdivided into purulent and putrid softening. This subdivision is based on the assumption that certain of the softened thrombi, *i. e.*, those classed as bland, are bacteriologically sterile, while the others are infected. The work of Harris and Longcope and Widál's researches on puerperal thrombosis have shown that bacteria are present in quite a large percentage of apparently bland thrombi, and this is often true even when no softening is present. Whether the softening of bland thrombi is due to infection is still an open question. From a clinical standpoint there is no question that emboli originating from softened thrombi do not all give rise to similar results, those from bland emboli causing a temporary febrile reaction and being comparatively harmless, while those from septic thrombi cause serious metastatic inflammations. It is possible that the bland softening is the result of an attenuated form of infection, although the fact that the escape of softened material into the circulation causes febrile reaction is not necessarily evidence that

infection is present. It is known that thrombi contain constituents originating from the blood itself which are capable of producing fever when introduced into the circulation. Of the definitely infective thrombi, the putrid differ from the purulent in that they are due to bacteria of putrefaction as distinguished from the ordinary pathogenic cocci.

Puriform softening is most common in cardiac thrombi, but may result in those occurring in peripheral vessels. In the so-called bland softening the liquefied material has to the naked eye the appearance of more or less blood-stained pus. The microscope shows that the puriform material is made up of the debris of the constituent elements of the clot, granular and fatty particles, blood pigment, crystals of fatty acid, and more or less degenerated red and white blood corpuscles. In the infective thrombi the softened area has the appearance of true pus and contains under the microscope numbers of polynuclear leukocytes and bacteria. In putrid softening the thrombus is of a greenish or brownish color, and the liquefied area has an offensive odor similar to that encountered elsewhere in association with gangrenous processes.

Localization of Thrombi.—*Cardiac Thrombi.*—Two types of cardiac thrombi are to be observed, the mycotic thrombi, usually of small size, associated with endocarditis, and the larger thrombus masses found in the cavities of the heart in connection with conditions of an infectious or cachectic nature or associated with enfeeblement of the circulation. The mycotic thrombi being directly due to endocarditis, usually occur on the valves, but are quite frequently mural, especially in the subacute form of endocarditis. The second type of thrombi, which occur especially in chronic heart disease with failure of compensation, form where the circulation is slowest and where the physical conditions favor the formation of eddies. Such conditions are found especially in the auricular appendages and in the apices of the ventricles between the columnæ carneæ. The peculiar cardiac thrombi known as ball thrombi, almost invariably occurring in the left auricle in association with mitral stenosis, are due to the detachment of portions of mural thrombi which become moulded to a spherical shape through accretion and constant rotation in the auricular cavity. They are of pathological rather than clinical significance, as are the curious pedunculated cardiac polyps which usually spring from the septum of the left auricle. Some of these are undoubtedly true organized thrombi; others are probably the result of intramural hemorrhage or are varicosities of the veins of the septum.

Arterial thrombi, commonly associated with chronic arterial disease or acute infectious arteritis, may occasionally accompany debilitating diseases or be due to trauma. They occur most frequently in the arteries of the extremities, particularly those of the legs, and involve the two sides of the body with almost equal frequency. The visceral arteries, especially those of the lungs, brain, heart, and intestines, are not infrequently involved, and sometimes main trunks like the aorta become thrombosed.

Venous thrombosis is by far the most frequent variety, as the mechanical and chemical conditions favoring thrombus formation are most frequently met with in the venous circulation. These conditions have been summarized by Welch as "the slower mean speed of the blood in veins than in

arteries; the low blood pressure; the flow from smaller into larger channels; the absence of pulsation; the presence of valves; fixation of the venous wall in certain situations to fasciæ and bone; the existence in some places of wide sinuses and ampullar dilatations; the agency of certain subsidiary forces, such as muscular contractions and movements of the limbs, in assisting the flow in the veins; the composition of venous blood, particularly the rich content of CO_2 , and perhaps the functions of the capillaries and small veins in the production and absorption of lymph."

Venous thrombi are found with the greatest frequency in the veins of the lower extremities, both superficial and deep, in the small pelvic veins, and in the cerebral sinuses. Thrombi in the veins of the arms are met with, and thrombi in the pulmonary veins are occasionally described. The venæ cavæ are, as a rule, only involved secondarily by the propagation of thrombi into them from their branches. A striking peculiarity of venous thrombosis is the marked tendency, both in the upper and lower extremities, to the involvement of the veins of the left side, probably due to a variety of factors. The causes generally adduced in connection with the leg are the greater length and obliquity of the left common iliac vein, its situation beneath the right common iliac artery, and the exposure of the vein on this side to pressure from the distended rectum or sigmoid flexure. The effects of posture in bedridden patients probably play an important part in accentuating the pressure factors and the lack of use of the limbs encourages feebleness in the venous circulation. The researches of McMurrich¹ indicate another important factor. He found in 10 out of 31 cadavers a localized adherence of the anterior and posterior walls of the common iliac vein just below its termination in the inferior vena cava. In 9 of 10 cases it occurred on the left side. McMurrich thinks it due to a developmental error. In like manner Hanot and Parmentier ascribe the frequency of left-sided thrombosis in the veins of the arms to an interference with the return flow of blood resulting from the greater length and obliquity of the left innominate vein. In the upper extremity Hirschlauff described developmental errors in connection with the valves near the junction of the internal jugular and subclavian veins analogous to those described by McMurrich in the iliac veins, and, like them, much more frequent on the left side. *Capillary thrombosis* is of pathological significance only.

Local Effects of Thrombosis.—These depend mainly upon the degree in which the circulation is obstructed by the thrombus. In cardiac thrombosis and in thrombosis occurring in saccular aneurisms there is usually no marked disturbance of the circulation, and there may be little or none from parietal thrombi in vessels, provided the vessel is a large one and the thrombus small. In the great majority of arterial and venous thrombi there is serious interference with the circulation, and the result depends mainly upon two factors; the rapidity with which the vessel is closed, and the number of collaterals entering the area whose nutrition is cut off. In the case of peripheral vessels the rapidity of closure is the more im-

¹ *Brit. Med. Jour.*, 1906, ii, 1699.

portant factor, as the vessels are usually well supplied with collaterals and there is free anastomosis. In the case of internal organs the character of the circulation is more important, for some organs have a terminal circulation in the anatomical sense and in others the amount of anastomosis is so slight that there is practically no chance for the formation of a collateral circulation. The gradual obliteration of an artery or vein by thrombosis is usually devoid of any result save the gradual development of a collateral circulation, although in some instances it may result in effects similar to those produced by a sudden stoppage of the circulation. The changes occurring from sudden stoppage of arterial blood supply from thrombosis are the same as those produced by embolism, and are so much more frequently the result of the latter complication that they are best considered under that head. Where obliteration of a vein of any size occurs suddenly, the most striking change is a venous or passive congestion followed by the escape of the blood serum into the tissues or the cavities of the body. There are records of rare instances in which thrombosis of the large venous trunks has been followed by gangrene, usually in patients the subjects of uncompensated cardiac disease with extreme feebleness of the circulation. In patients with thrombo-phlebitis, besides the purely mechanical effects of stoppage of the circulation, the local evidences of inflammation occur, with the usual clinical picture. In some instances, where the infection is intense, actual abscess formation about the thrombosed vein results. This is rather unusual in connection with the peripheral vessels, but is common enough in some situations, as in the branches of the portal vein.

Symptoms.—These will depend to some extent on the same factors which influence the effects of the process on the tissues, viz., the rapidity with which the circulation is cut off and the extent of the collateral circulation in the affected tissue. Certain local peculiarities in the vascularization of organs and in the sensitiveness of their cells to interference with the blood supply are also factors in causing variation in the symptoms. There is a certain percentage of thrombi in the peripheral vessels associated with gradual occlusion of the lumen which produce no symptoms whatever, and thrombi in the vessels of the internal organs are frequently latent or give rise to no clinical signs which permit of a diagnosis. Von Schrötter divides the symptoms of thrombosis into those which are directly due to the formation of the thrombus and those which result from its effect on the blood supply. Of the former group *pain* is the most prominent, of the latter *œdema* or fluid in the cavities of the body. General symptoms, such as febrile reaction and quickened pulse, are also common. The symptoms of thrombosis vary so much according to the situation that it is necessary to consider the more prominent forms in detail.

Peripheral Venous Thrombosis.—This is the most common variety, and as the femoral vein is the most frequent site of the process, thrombosis of this vessel will be described. Premonitory symptoms and signs may occur many days before a discoverable thrombosis in some instances. As Conner has pointed out, these are usually pulmonary, and due to the lodgment of small emboli. The patient is apt to complain of sudden

pain in the side with dyspnoea and cyanosis. Cough is at times present, and may be accompanied by bloody sputum. The temperature is little if at all affected. The signs vary from those of slight localized pleurisy to those of a fairly extensive plastic effusion, or localized consolidation of the lung may occur. In some instances chills may occur prior to the development of thrombi. The so-called "kletter puls" (climbing pulse) of Mahler has been shown to be unreliable as a premonitory sign, and Michaelis' premonitory period of subnormal temperature is also of doubtful value.

In a typical case both general and local symptoms are present. The general symptoms often precede the local ones, and the onset of the attack is at times a definite *rigor*. More commonly there are chilly sensations followed by fever and perhaps sweating, and an increase in the rapidity of the heart's action. The *fever* in patients with bland thrombi is not usually high, 101° to 102° F., in an average case; in infective thrombosis it may be much higher, 104° or 105° F. Sweating is a rather common accompaniment of the fever, but is not always present. Examination of the blood at the onset of the thrombosis will often show a pure *leukocytosis*, although in diseases like typhoid fever, in which a leukopenia is the rule, the rise in the number of leukocytes may be slight or lacking. Not infrequently these general symptoms precede the local symptoms by several days.¹

The most prominent local symptom at the onset of thrombosis is *pain*. In femoral thrombosis this often appears first in the calf, although it may be present from the beginning at the site of thrombus formation. The pain is often intermittent at first, but gradually becomes constant. It may not be very severe, but may be intense, and is described sometimes as burning or boring, sometimes as cramp-like. At first localized, it usually becomes more general as the disease progresses. Frequently the patient complains of a feeling of tension and weight in the limb. The pain is associated with tenderness of the affected member, most marked along the course of the thrombosed vessel, which can often be rolled under the fingers as a firm, sensitive cord. In spare individuals with thrombosis of superficial veins the course of the vessel may be traceable as a dull, red line on the overlying skin, usually rather wider than the diameter of the vein. Disturbances of sensation are uncommon, aside from feelings of numbness and formication. In some patients, however, there may be intense neuralgic pains, especially in the domain of the sciatic nerve, and these are apparently due in some instances to a definite neuritis. Disturbance of motion is usually present, due to the natural tendency to immobilize the limb.

Œdema is the second prominent local symptom. Like the pain, it may appear first in the region of the calf and gradually extend upward, but in patients in whom infective thrombosis is present and in whom inflammatory œdema predominates, it may begin about the site of thrombosis and extend toward the periphery. The degree of œdema varies considerably; it may be very slight, but in well-marked femoral throm-

¹ When the sensorium is obtunded, as in severe typhoid fever, there may be no complaint of pain.

bosis is generally a prominent feature. Its character varies to some extent with the type of thrombosis; in patients with marantic thrombosis or with mild thrombo-phlebitis the affected limb is usually pale, with a glossy skin, and cooler than its fellow. Occasionally there is marked cyanosis, and frequently the superficial veins are dilated. In the severer infective types of thrombo-phlebitis the skin may be reddened, and the surface temperature of the affected limb may be considerably higher than that of the unaffected one. The œdema does not usually pit as easily as the œdema of heart and kidney disease, but is firm and elastic.

In typical cases there may be considerable variation from the above picture. The affection may be entirely latent. Almost any of the symptoms and signs may be absent. The constitutional symptoms, especially in old, feeble individuals with cachexia, may be lacking. The pain may be absent or so slight that it is entirely disregarded or attributed to some other cause. The œdema may be so slight that it is overlooked. It is usually in thrombosis of the deeper and smaller veins, such as those of the calf, that the entirely latent forms occur. Thrombosis of larger veins may be disregarded by the patient, but will usually be discovered by a careful observer. The signs may be masked, as in cardiac disease, by changes like œdema due to the original malady. On the other hand, the general symptoms, especially in the primary infective thromboses, may be intense and partake of the character of a violent sepsis.

The *course* of peripheral venous thrombosis varies considerably with the nature of the exciting cause and of the disease which preceded this complication. In cases associated with severe sepsis or with the terminal stages of debilitating diseases, death often takes place before a chance for retrograde changes is offered. In the ordinary thrombosis accompanying infectious diseases, in which recovery follows, the acute symptoms usually begin to subside by the end of the first week, the pain and tenderness become less severe after four or five days, the œdema becomes less marked, and the fever and constitutional symptoms abate. Where the local infection is severe the subsidence of active symptoms is often much slower. The lasting effects upon the limb will be considered under complications. The thromboses of the upper extremities are often less severe and recover more quickly than those of the lower extremities.

The *diagnosis* of peripheral venous thrombosis is, in characteristic cases, a simple matter. The sudden onset with localized pain, the palpable tender vessel, the evidence of disturbance in the venous circulation, and the œdema make recognition easy. In patients with thrombosis of small, deep-seated veins, when the vessel is not palpable and there is no marked œdema, diagnosis is more difficult. The differentiation from embolism will be discussed under that head; it is only necessary to say here that in thrombosis the arterial pulsations can still be felt, and that gangrene, so common in embolism, is very rare in thrombosis.

Thrombosis of the Superior Vena Cava.¹—The majority of instances are associated with compression of the vein by tumors, aneurism, or chronic inflammatory disease involving the vessel in cicatricial tissue. The

¹ Osler, *Johns Hopkins Hosp. Bull.*, 1903, 14, 169.

symptoms depend on the degree of establishment of the collateral circulation and in most instances the immediate consequences of the thrombosis are so severe that death rapidly ensues. Osler states that the clinical picture in individuals who survive and establish a collateral circulation appears under one of two types. In one class of cases the patient has for years complete compensation with good health, followed by the sudden appearance of urgent symptoms, usually attacks of dyspnoea with recurrent effusion into the pleural cavities. In the second group symptoms of obstruction of the venous circulation are constantly present. In Osler's first case there was pain in the chest with swelling of the face on exertion, cough, and cyanosis. The patient died of tuberculosis. Dilatation of the superficial veins is a prominent feature in these cases. The veins concerned in the collateral circulation vary according to the situation of the thrombus. If this occurs distal to the azygos vein the collateral circulation takes place, according to Forel, mainly through this vessel. In Osler's case there was marked enlargement of the lateral thoracic veins and the superficial epigastric veins which carried the blood from the subclavian into the common iliacs.

Thrombosis of the Inferior Vena Cava.—Autochthonous thrombi are rare in the inferior vena cava and thrombosis usually results from propagation of thrombi from affluents, or from compression of the vein by neoplasm, aneurism, or the products of inflammation. Thrombosis occasionally results from compression at the point of passage through the diaphragm as the result of sagging of this muscle from the weight of a left-sided pleural exudate. Disease of the vessel wall, either simple phlebitis or new growth, may cause thrombosis of the vena cava, and occasional instances after the infectious diseases have been noted. Compression by the enlarged head of the pancreas is a rare cause.

Thrombosis of the inferior vena cava, even when complete, may fail to produce symptoms in old or prostrated individuals in the terminal stages of some debilitating disease with great enfeeblement of the circulation. Usually there is a well-marked œdema of the lower extremities, especially of the back, without ascites. The œdema may be unilateral, as has been noted by Schlesinger. This may be due to congenital duplication of the vena cava or some peculiarity in the communication between the veins of the upper and one lower extremity. It may occur because the thrombus in the vena cava is propagated from the iliac on one side, is parietal, and does not occlude the other iliac. Sometimes the œdema does not occur on one side because an old thrombus of one iliac vein has led to the formation of a collateral circulation. Involvement of the renal veins may cause a diminution in the secretion of urine, with albuminuria and hematuria, but, as Welch points out, these symptoms do not always appear. Involvement of the hepatic veins may lead to portal obstruction with enlargement of the liver, splenic tumor, and ascites. In patients who survive, an extensive collateral circulation is established. This may involve only the deeper veins, rendering diagnosis impossible, or more commonly the superficial veins of the groins and trunk take part. In cases with the superficial compensatory circulation the communication between the affluents of the inferior vena cava and the supe-

rior vena cava is carried on by the epigastric veins, the circumflex iliac veins, the long thoracic veins, the internal mammary veins, the intercostal veins, the external pudic vein, and the lumbovertebral anastomotic trunk of Braune. The deep anastomosis is carried on by the azygos and hemi-azygos and the lumbar veins.

Thrombosis of the Renal Vessels.—This will be considered with embolism, as the results are the same. Thrombosis of the renal veins is not infrequent and may be autochthonous, then usually associated with renal disease or debilitating conditions, or may be due to the extension of a thrombus from the inferior vena cava.

In many instances thrombosis of the renal vein is not followed by marked symptoms. Welch states that it is the exception for a patient to present symptoms referable to the lesion. This lack of symptoms is most likely to be present when the thrombus forms gradually, as there are abundant anastomotic channels and a collateral circulation is rapidly established. In some patients thrombosis of the renal veins is followed by symptoms so definite that a diagnosis may be made without difficulty. Briefly stated, the more important symptoms are pain in the region of the kidney, marked albuminuria, usually accompanied by hematuria and decreased amount of urine with a high specific gravity, and an enlarged, tender, palpable kidney. The pain may be very severe and may persist for weeks. Long after its disappearance the kidney may still be tender on palpation. The increase in size of the kidney may be very considerable, and it may be a simple matter to palpate it. The albuminuria is the most constant urinary change, and the amount of albumin may reach as high as fourteen per mille by Esbach's albuminometer. In patients who recover, albumin may be present after a period of two or three months. Hematuria is not constant and is said by Hutinel to be much less liable to occur in children than in adults. It may be marked enough to be evident on examination of the urine with the naked eye. It persists a much shorter time than the albuminuria, usually disappearing in a week or two. Fever and the accompanying constitutional symptoms occur with thrombosis of the renal veins in some instances. Bilateral thrombosis of the renal veins leads to anuria followed by death.

Thrombosis of the Mesenteric Vessels.—Thrombosis of the mesenteric veins may either be secondary to portal thrombosis or may originate as a primary process in the branches of the veins. The primary form may be due to local or to general causes. The local causes take the form of inflammatory lesions of the intestinal wall, such as ulcers, or occur as enlarged mesenteric glands or pancreatic or gastric tumors causing thrombosis from compression. Occasionally local disease of the vessel wall, either simple phlebitis or luetic inflammation, is present. Of the general causes the infections, and especially typhoid fever and the various forms of sepsis must be mentioned. Thrombosis of the mesenteric vein not infrequently follows embolism of the arteries.

The *symptoms* of thrombosis are essentially the same as those following embolism of the mesenteric arteries except that they are, if anything, more severe. In 5 out of the 157 cases collected by Jackson, Porter, and

Quinby,¹ there were no symptoms referable to the abdomen. The most prominent symptoms in the average case are pain, nausea and vomiting, either diarrhoea or constipation, or both at different stages, abdominal tenderness, and signs of intestinal obstruction. Abdominal *pain* is present in the great majority of instances, and in over one-half of the patients is general in character. Localized pain when present is most common in the upper abdominal zones, either in the epigastrium or about the umbilicus. Radiation of the pain is fairly common, but there is no particular distribution which is characteristic. The onset of the symptoms is usually sudden, and there is often a constant dull ache with exacerbations of severe colic. The cause of the pain is thought to be the contraction of the intestinal wall, and its spasmodic character makes it analogous to the pain of angina pectoris or to attacks of intestinal colic from abdominal arteriosclerosis (angina abdominis). Nausea and vomiting are not necessarily present, and are more apt to be severe when the thrombosis occurs suddenly. The character of the vomitus depends on the severity and duration of the case, normal stomach contents being vomited early; later bile, fecal material, or even pure blood. Diarrhoea is present in only 50 per cent. of the patients, and in 41 per cent. blood occurs in the stools at one time or another. The diarrhoea is preceded or succeeded by obstipation in a small percentage of patients. Obstipation alone occurred in 22 per cent. of the cases collected by Jackson, Porter, and Quinby. It is at times followed by diarrhoea, usually with bloody passages. Abdominal tenderness occurs in 70 per cent. of the patients, and in a large majority is, like the pain, generalized. When localized it is most likely to occur about the umbilicus, in the cecal region, or in the epigastrium. Distention is a late symptom and is practically always generalized. Leukocytosis and iodophilia were present in the Boston cases. The temperature varies; it may fall below normal, but not infrequently fever is present. Rare signs are glycosuria and purpura.

The *diagnosis* is usually difficult, inasmuch as in but few cases the majority of the symptoms are present. In a large number of cases the diagnosis of intestinal obstruction is made. The most characteristic signs are stated to be the sudden onset of colicky abdominal pains with a fall in the temperature and passage of blood-stained stools, and later symptoms of intestinal obstruction with distention of the abdomen and perhaps some ascites. Thrombosis of the mesenteric veins is not infrequently associated with thrombi elsewhere in the body, and may be directly secondary to portal thrombosis. The presence of such thrombi elsewhere or of symptoms referable to thrombi should make the diagnosis more simple. Aside from intestinal obstruction, the condition may be confounded, on account of the vomiting and passage of blood, with gastric or duodenal ulcer or with disease of the heart and liver, accompanied by passive congestion in the abdominal organs. Differential diagnosis in these cases must rest upon the presence of other signs of these diseases. Patients in whom purpura is present in association with thrombosis of the mesenteric veins might be confused with instances of abdominal crisis in connection with purpuric skin eruptions of the erythema group.

¹ *Jour. Am. Med. Assn.*, 1904, **42**, 1469 and **43**, 25, 110, 183,

Thrombosis of the Portal Vein.—This may result from disease in the vein itself or much more commonly from pathological processes which cause compression of the vessel. In the vessel wall a sclerotic process comparable to arteriosclerosis has been occasionally described, but is quite rare. Usually portal thrombi not due to external pressure are of the propagated variety, are often although not necessarily septic, and are commonly associated with intra-abdominal inflammatory processes, especially appendicitis. Thrombosis from pressure may occur in connection with neoplasms of the head of the pancreas, the stomach, the omentum, or the lymph nodes in the hilum of the liver. Another group is associated with compression by cicatricial tissue either within the liver, as in cases of cirrhosis, or external to that organ, but surrounding the portal trunk. In the latter instance the scar tissue results from a localized peritonitis which may be due to gall-stones, gastric or duodenal ulcer, or tuberculosis. Gall-stones themselves have occasionally been situated so as to compress the portal vein and lead to thrombosis. A certain number of instances of portal thrombosis without apparent cause have been recorded, the so-called idiopathic portal thrombosis, but Ponfick thinks that some of these are traumatic.

The *symptoms* of pylethrombosis are very different in septic and non-septic cases. Septic or suppurative pylephlebitis results in the formation of multiple abscesses in the liver, and the outcome is usually a rapid and fatal termination. *Appendicitis* is so frequently the exciting cause of this form of portal thrombosis that the French school speak of it as “le foie appendiculaire.”¹ The clinical picture is that of sepsis with local symptoms pointing to the liver. The onset is often sudden, with a violent chill, high fever, and profuse sweating. The fever persists during the course of the disease, but is usually marked by exacerbations, often with chills, which may occur daily at about the same period, or may be more frequent and irregular. Quite early, as a rule, gastro-intestinal symptoms appear, nausea and vomiting with perhaps diarrhoea, which according to Dieulafoy¹ may be paroxysmal. Constipation may, however, be present throughout. Jaundice and tenderness in the region of the liver are usually prominent signs, and as the disease progresses the liver may reach twice its normal size. The icterus varies in intensity, and may appear early in the disease or not until late. The patients finally pass into a typhoid state and die in collapse or may succumb with the symptoms of cholemia.

The form of portal thrombosis associated with simple pylephlebitis gives rise, in the majority of instances, to a clinical picture resembling that of atrophic cirrhosis of the liver. In some patients, as in the remarkable one reported by Saxer,² most extensive thrombosis of the main branches of the portal vein may occur without characteristic symptoms. Usually enlargement of the spleen, ascites which recurs rapidly after tapping, and the formation of a collateral circulation are prominent features. The collateral circulation may involve the superficial veins of the abdomen and lower chest, and is then plainly apparent, or it may occur

¹ Dieulafoy, *Clinique Médicale de l'Hôtel Dieu*, 1897–98.

² *Cent. f. allgem. Path.*, 1902, **13**, Nr. 15.

through the left coronary vein of the stomach, the œsophageal veins, the intercostal veins, and the azygos veins. In the latter instance large varices may form beneath the mucous membrane of the stomach or lower end of the œsophagus, and such patients are apt to suffer from sudden and severe hematemesis or melena. The ascites which is so prominent a feature in some patients may be lacking in those in whom such hemorrhages occur. On the other hand, patients with well-marked ascites do not usually have the gastric and intestinal hemorrhages. The minor manifestations of portal obstruction, anorexia, nausea, and intestinal disturbances, may be present, especially in long-standing cases. Jaundice does not occur unless complications are present. A few patients recover as the result of the formation of a fully compensating collateral circulation, but as a rule a fatal termination is to be expected either from severe gastric or intestinal hemorrhage, from gradually increasing asthenia or from extension of the thrombosis or involvement of the mesenteric vessels and infarction of the intestine. When the process comes on gradually and gives rise to a picture of chronic portal obstruction, it may be impossible to differentiate it from atrophic cirrhosis of the liver, especially as this organ is often, although not invariably, decreased in size in cases of portal thrombosis. In the acute cases the rapid onset in an individual with a previously clean record, the absence of an alcoholic history, the absence of decrease in size of the liver, or even the enlargement of this organ, the early appearance of ascites and its rapid recurrence after tapping, or the presence of severe gastric or intestinal hemorrhages—all suggest a portal thrombosis rather than cirrhosis.

Thrombosis of the Hepatic Veins.¹—Attention has been called, especially by Chiari and his pupils, to a form of thrombo-phlebitis of the hepatic veins which is probably not very uncommon. It may be overlooked because the symptoms and gross pathology are essentially those of hepatic cirrhosis. The disease attacks both sexes alike, usually during young adult life, and seems at times to develop upon a luetic basis. Postmortem examination shows in most cases an obliterating endophlebitis of the hepatic veins usually associated with thrombosis. Not infrequently thrombi are also present in the branches of the portal vein.

The *symptoms* as a rule appear gradually, although in rare cases an acute onset with death in less than two weeks has been noted. Usually a sense of pain and discomfort in the hepatic region or the upper abdomen is the first thing noted. Later symptoms suggestive of atrophic cirrhosis occur, the abdomen gradually enlarges, ascites develops, and gastrointestinal disturbances may appear. The signs of a compensatory circulation may be apparent in the form of a caput medusæ. Hematemesis and melena occur in rare instances, much less commonly than in portal thrombosis. Hematuria has been occasionally noted. Examination shows the presence of fluid in the abdominal cavity, which if withdrawn, rapidly reaccumulates. It usually has the characteristics of a simple transudate but is occasionally hemorrhagic. The liver is enlarged, smooth, and firm, in the early stages; later it becomes contracted and

¹ Hess, *Am. Jour. Med. Sci.*, 1905, **130**, 986; Umbreit, *Virchow's Archiv.*, 1906, vol. **183**.

more or less nodular. Jaundice is generally absent. The spleen is enlarged, hard, and easily palpable. In the final stages general anasarca may appear. There is as a rule no fever, and the urine is negative. In most patients the course is shorter than that of an ordinary cirrhosis, the average duration after the onset of symptoms being about six months.

Hess states that no case of this disease has been diagnosed during life, most patients having been considered to be suffering from cirrhosis of the liver. Two acute cases with marked gastro-intestinal symptoms and prostration were diagnosed as poisoning in one instance and intestinal obstruction in the other. According to Hess, the main points in distinguishing hepatic thrombo-phlebitis from cirrhosis are its occurrence in younger individuals, the absence of the cause of cirrhosis, the presence of pain in the hepatic region, the rapid development of ascites, and the frequency with which paracentesis is needed.

Thrombo-phlebitis of the Umbilical Veins.—The occurrence of infection of the umbilical veins in the newborn child is one of the most serious diseases of early life. The condition is often insidious in onset, for, as a rule, there are no marked local signs in the umbilical stump. In occasional complicated cases pus can be squeezed from the severed end of the vein, but this is exceptional. It is stated by some observers that the more severe the infection the less the likelihood of marked local symptoms. Usually the symptom which calls attention to the condition is a gradually intensifying jaundice, which is often accompanied by symptoms of sepsis. Later hemorrhages may occur, most often from the stump of the umbilical cord. Fever may be marked. There may be inflammation of the serous membranes, pericarditis especially, and occasionally gangrene of the umbilical stump, or erysipelas of the skin surrounding it. The inflammation usually extends to the veins of the liver and causes a diffuse hepatitis or multiple abscesses of the liver. The prognosis is very grave, much more so than that of the more frequent umbilical arteritis.

Thrombosis of the Vessels of the Spleen.—Thrombosis of the main trunk of the splenic artery occurs very rarely, although this vessel is frequently the seat of arteriosclerosis. Thrombi in the smaller arterial branches give rise to the same symptoms as emboli, and will be considered under that head. Thrombosis of the main trunk of the splenic vein is rare. Thrombi in the smaller branches of the vein occasionally cause infarcts. Septic thrombosis of the splenic vein may occur in connection with infectious processes in the pancreas from the contiguity of the vessel to that organ. The vein may be thrombosed as a result of typhoid fever. Eppinger and Ranzi called attention to the fact that an attack of thrombosis of the splenic vein may be febrile and accompanied by pain in the splenic region. Such patients develop, years after the thrombosis, a chronic enlargement of the spleen with a marked tendency to hematemesis. The condition is to be distinguished from splenic anemia.

Thrombosis of the Pulmonary Vessels.—Thrombi in the pulmonary veins are common enough in the areas involved in inflammatory conditions of the lung, infarcts and tumors, and in emphysema. They occasionally give rise to emboli in the systemic circulation. Thrombi in the pulmonary arteries, even when they cause blocking of medium-sized branches, often,

as Newton Pitt pointed out, give rise to no marked changes in the lung. When changes occur they resemble both clinically and pathologically those due to embolism, and will be considered under that head.

The occurrence of *arterial thrombosis* has been discussed to some extent under the heading of various diseases concerned in its etiology. The symptoms so closely duplicate those of embolism that the two conditions will be considered together.

Thrombo-angiitis Obliterans.—The importance of this form of thrombosis has been emphasized by Erb in Germany and Buerger in New York. The condition is characterized by the formation of parietal, red thrombi, especially in the arteries of the lower extremities, which tend to organize and to lead to the production of a collateral circulation when complete obstruction occurs. The veins, also, are involved, and in some instances recurrent attacks of thrombo-phlebitis simulating phlebitis migrans occur in these vessels. The process is very much more prevalent in the male than in the female sex, usually occurs after forty, is especially likely to attack Jewish people, and is possibly associated with exposure to changes in temperature and the excessive use of tobacco. Syphilis plays a doubtful part in the etiology.

There are two main clinical manifestations: (1) The condition usually described as intermittent claudication or intermittent limping, and (2) juvenile or presenile gangrene. In typical cases with *intermittent claudication*, the patient complains, on attempting to walk fast, of paresthesia and pain in the feet, tension, pain, and stiffness in the calves, coldness of the feet, and increased difficulty in walking which finally results in the severer cases in the patient stopping to rest. After a period of rest, the patient is able to proceed but any attempt at hurry results in a recurrence of the symptoms. Examination reveals diminution or absence of pulsation in the arteries of the feet, often associated with definite thickening of the vessels and with certain vasomotor phenomena. When the limb is elevated the foot becomes pale, when the patient sits with pendant feet marked redness to blueness of the soles, sometimes of the greater part of the feet, develops. In some cases the vasomotor changes closely simulate erythromelalgia or Raynaud's disease.

The second type of case is characterized by *gangrene* of the lower extremities, occurring at an age much earlier than that at which senile gangrene appears. The gangrene may be preceded by the manifestations of intermittent claudication or it may appear spontaneously. Symptomatically it does not differ from other forms of gangrene. It is associated with severe pain, and the affected portions present the cold blue appearance and subsequent necrosis characteristic of other forms of gangrene. The pain is so severe, in fact, that it is not unusual for the patient to implore the surgeon to remove the limb.

Capillary Thrombosis.—This is of pathological rather than clinical interest. The possible relationship of capillary thrombi in the kidney glomeruli to disturbances in the secretion of urine, as suggested by Welch, seems worthy of further investigation. The relation of capillary thrombi to gastric hemorrhage and to ulcer and the so-called gastric erosions has been suggested by von Eiselberg and others, but needs confirmation.

Cardiac Thrombosis.—The diagnosis of the ordinary parietal cardiac thrombi from any direct effect they may produce upon the heart itself is generally considered to be impossible. The presence of parietal cardiac thrombi may be suspected when, during failure in compensation without distinct evidences of valvular endocarditis, symptoms of embolism occur in organs supplied by the systemic circulation. Pedunculated thrombi and ball thrombi may be associated with sudden death with symptoms of syncope. In other instances ball thrombi are believed to give rise to symptoms which permit of a possible diagnosis, although it is doubtful if a correct diagnosis has been made during life. The symptoms are essentially those of an exaggerated mitral stenosis, marked dyspnoea, cough, an unusually feeble pulse, and evidences of venous engorgement out of proportion to the degree which is usual in uncomplicated mitral stenosis. Localized gangrene of the foot, which von Ziemssen described in his patients and considered almost pathognomonic, is not necessarily present. The physical signs are those of mitral stenosis, although the presystolic murmur is said to be absent in some instances, and, when present, to show a marked tendency to intermittency. As diagnostic points, von Ziemssen emphasizes the physical signs of mitral stenosis, the occurrence of the ordinary clinical signs of this lesion is an exaggerated form, especially a very small and feeble pulse, and circumscribed gangrene of the foot.

Sequelæ of Thrombosis.—Aside from those instances in which the symptoms essentially represent the sequelæ of thrombosis, as in thrombosis of the portal or hepatic veins, the remote results of thrombosis of the vessels of the internal organs are as a rule unrecognizable, for if the changes in the affected organ are not sufficient to cause death they are subsequently compensated for by the unaffected portions of the viscus, or, in cases of paired organs, by the uninvolved one. Changes in the central nervous system due to thrombosis are not, of course, followed by recovery of function if the lesion is at all extensive. Certain remote effects of peripheral thrombosis, and especially of peripheral venous thrombosis, need brief discussion. Of peripheral arterial thrombosis it need only be stated that the sequelæ are the same as of arterial embolism.

The important sequelæ of peripheral venous thrombosis may be considered under two heads: first, the occurrence of secondary embolism, and, second, the local effects. The factors which influence secondary embolism have already been briefly discussed in connection with the disease associations of thrombosis. As a general rule septic thrombi are more apt to give rise to secondary emboli than bland ones, and certain forms of thrombosis are commonly associated with embolism, while in others this sequel is almost unheard of. Thus puerperal thrombosis commonly results in secondary embolism, while syphilitic thrombosis almost never does so. Typhoid thrombosis is one of the forms in which secondary embolism is rather unusual, as it is in idiopathic recurrent thrombosis. Small pulmonary emboli may not infrequently precede the clinical recognition of typhoid thrombosis as Conner has pointed out. Large pulmonary emboli are rare. There is, too, apparently some difference in the likelihood of embolism according to the vein affected. Haward's table shows secondary embolism most frequently after thrombosis

involving the iliac veins, next in frequency after saphenous and femoral thrombosis, and only occasionally after thrombosis of the veins of the leg or of the viscera. The fact that the danger of embolism can be greatly increased by sudden movements on the part of the patient or by undue manipulation of the affected vein should be kept in mind.

Of the local complications of peripheral venous thrombosis, the perivascular suppuration has already been mentioned. Much more important are the more or less disabling sequelæ which may occur when a large vessel like the femoral is permanently plugged. In patients who have suffered from such a lesion there may be present for years, even during the remainder of life, certain annoying symptoms. The most common of these are a feeling of heaviness and clumsiness in the limb, œdema, especially at night and after exercise, stiffness of the joints, and impairment of the circulation with coldness of the member. Changes in the muscles of the limb, usually in the form of atrophy, are frequent; rarely a well-marked hypertrophy of the muscles results. To these symptoms must be added pain, which may be present along the course of the thrombosed vessel or may be more widespread, and is especially apt to invade the territory of the sciatic. Usually slight, the pain may be intense, neuralgic in character, and quite intractable. At night or after exertion distressing cramps in the muscles may be present.

Diagnosis and Prognosis.—The diagnosis and prognosis of thrombosis vary so much according to the disease associations and the vein affected that a general discussion of the subject is impracticable. The main points will be found in the discussion of the disease associations and of the symptomatology of thrombosis of different vessels.

Treatment.—This practically resolves itself into the treatment of peripheral thrombosis and of one or two forms of visceral thrombosis in which operative interference may with propriety be essayed. The *prophylaxis* of thrombosis has not as yet been seriously considered, and it is hard to see how this can be done unless we are to regard all patients suffering from certain diseases as possible candidates for this complication. We have as yet no way of telling what patients are likely to develop thrombosis, nor are we sure that the underlying factors are the same in all instances. It is, however, in view of the importance of the static element in spontaneous thrombosis, essential to consider the necessity of preventing patients from remaining for long periods in cramped positions and, in the case of surgical operations, to avoid keeping the patient in bed longer than is necessary.

The immediate treatment of patients with peripheral thrombosis consists of the immobilization of the limb and in such symptomatic treatment as is demanded. The limb must be placed in a comfortable position and the immobility must be absolute, the necessity for this being strongly impressed both upon the patient and the attendants. So far as the patient is concerned, he must not only be warned against sudden movements, but also against straining at stool and excessive coughing, and if necessary, laxatives or pulmonary sedatives may be administered to aid him. Mechanical methods must be employed to fix the limb, and at the same time pressure in the immediate neighborhood of the thrombosed

vein must be avoided. This may be done by the application of a well-fitting, properly padded splint, or, after wrapping the limb in cotton wadding, by fastening it to the mattress by means of bandage strips. The use of bandage strips has the advantage over the use of the splint of allowing easy access to the limb with a minimum of manipulation. The only symptom likely to demand treatment at the onset is *pain*, which may be intense. Morphine hypodermically is the only remedy of value in severe cases but its use is seldom necessary after two or three days. This general treatment may be supplemented by the local application of an ice-bag or of hot fomentations. Belladonna ointment applied along the course of the vein or 30 per cent. ichthyol in lanolin has been recommended. The application of cold compresses moistened with normal saline solution for two or three hours daily during the second week is also recommended, as are applications of lead and opium lotion. All local medication should be applied with the greatest care.

In the treatment of peripheral thrombosis after the acute symptoms have subsided the important question to be decided upon is how long absolute immobility is to be maintained. The French writers especially insist that many of the ordinary local sequelæ may be avoided by beginning passive motion and massage early. The three indications for beginning active treatment are, according to Quénu,¹ absence of fever for three weeks, disappearance of local tenderness over the affected vessel, and progressive decrease in the œdema. The plan outlined by this writer is as follows: During the first week that movement is permissible, only passive motion is allowed, consisting of gentle superficial rubbing and gentle movement of the different joints of the affected limb. During the second week massage of the muscles, avoiding the region of the vessel, and more marked passive motion of the joints are employed, although marked flexion of the joints in the neighborhood of the thrombus should be guarded against. During the third week the restraining bonds or splint may be gradually removed, so that at the end of this week all mechanical restraint has been removed and the patient is allowed to move the limb gently in bed. During the fourth week the patient may be allowed to increase the movements of the limb in bed, and finally to get up. The limb should at first be supported by a bandage, preferably one of some light elastic tissue, as heavy stockings may hinder the formation of the collateral circulation. The use of some support, preferably a cane, will be necessary when the patient begins to walk, but may be discarded as power and confidence are regained.

In patients in whom œdema and pain persist for a long time after convalescence, these may require special treatment. For the œdema the use of massage and electricity and the wearing of a light supporting bandage are necessary. For the pain the application of tincture of iodine over the painful points, local warm douches or warm baths, and electricity are of value. The last remedy may be applied in the form of the high-frequency current, or if pain is not very marked the constant current in doses of from 25 to 50 ma. may be passed through the limb for some fifteen or twenty minutes daily. Faradization applied so as to produce inter-

¹ *La Semaine medicale*, July 26, 1905.

mittent contractions of the muscles over a period of ten to fifteen minutes daily may be of use in some patients in whom the pain is slight. According to Cleaves, electrical treatment should be begun during the latter part of the acute stage of thrombosis. The continuous current is first used in doses not to exceed 5 ma. for a few minutes daily. The current must have an unvarying rate of change, and must be capable of producing long, wave-like, undulatory, muscular contractions. In chronic cases when a whole leg or arm is stiff and œdematous, the indifferent contact is best made at first by placing the foot or hand in a 1 per cent. saline bath at 100° F. charged from the indifferent pole. The active contact is made by a hand electrode which is passed over the affected limb. After a week or two the indifferent contact may be placed over the lumbar enlargement so as to apply the stimulant directly through the nerve supply. Treatment should be applied at first daily for ten minute doses of 8 ma., gradually increased as the treatment progresses to 20 ma. The treatments may be reduced in number after the first two weeks, first to two or three a week and later to weekly treatments. Usually from one and a half to three months' treatment is necessary. The sinusoidal current may be used as an adjunct during the later stages of the treatment. Internal medication is of no value except in special forms such as luetic thrombo-phlebitis.

The surgical treatment of peripheral thrombosis has been suggested by Moullin in patients in whom the superficial veins are involved, and by Briggs in idiopathic recurrent thrombo-phlebitis. Moullin¹ has been in the habit of excising the whole thrombosed vessel in such cases, and claims that it shortens the period of illness and removes the risks of secondary embolism, deep thrombosis from extension, and recurrence in the same vessel. There seems no reason why his method should not be more extensively employed in selected cases.

Treatment of thrombosis of *visceral vessels* must in most instances be purely symptomatic. The chances of detachment of emboli from thrombi in visceral veins is slight; nevertheless, absolute rest in bed should be required when visceral thrombosis is suspected. In the case of mesenteric and portal thrombosis, there is hope that operation will save a small percentage of patients. The mortality after operation is high but without operation the patient is almost certainly doomed, and with increased skill in diagnosis and improved technique the percentage of successes can doubtless be increased. The operation should be quickly performed with a minimum chance of shock. The procedure recommended by Jackson, Porter, and Quinby, *i. e.*, bringing the involved intestine into the wound, resecting with liberal margins, and fixing the open edges in the wound, seems most logical. It is possible that the Talma operation or permanent peritoneal drainage might be of value in thrombosis of the portal or hepatic veins provided a diagnosis could be made early enough.

*Treatment of Thrombo-angiitis.*²—The treatment of thrombo-angiitis obliterans requires separate consideration. If the disease is recognized

¹ *Brit. Med. Jour.*, 1904, ii, 1688.

² For full details See Buerger, Leo. *The Circulatory Disturbances of the Extremities*, 1924, W. B. Saunders Company, Philadelphia.

in an early stage it may apparently be held in check to some extent by physical inactivity. I have knowledge of one patient who, by confining his walking to the house, maintained his condition unchanged for five or six years. Avoidance of tobacco and protection of the limbs against cold and damp are also necessary preventive measures as is the avoidance of constricting garters and tight shoes. Anything which causes lowering of the general or local blood-pressure is also to be shunned; in one patient seen several years ago gangrene of the foot followed immediately after a prolonged Russian bath. Extreme cleanliness of the feet is necessary in these patients for infection very easily gains a foothold in the poorly-nourished tissues and traumata, even of a trivial nature, may result in gangrene. Home treatment of corns and ingrowing toe nails, associated as it usually is with the use of non-sterile instruments, may be the starting point of an uncontrollable necrotic process.

For the treatment of the *pain* radical procedures like posterior root resection or injection with absolute alcohol are of dubious value. Opium in some form is usually necessary in the severe cases but must be used with great caution to avoid habituation. The various treatments aimed at improving the circulation may lead to temporary relief.

The various procedures used in an attempt to cause an amelioration of the process all have in view improvement in the circulation either by mechanical or chemical means. Buerger's method of inducing postural hyperemia is of distinct value in some cases. Heat in the form of baking, the electric thermaphore or diathermy is also of value but should not be applied to parts of the limb showing acute phlebitis, ulceration or gangrene. The injection of solutions into the blood, such as Ringer's solution or sodium citrate, with the object of reducing blood viscosity is of doubtful utility. A few patients obtain temporary relief following perivascular sympathectomy according to the method of Leriche.¹ Drugs are of no value in my experience though mercurials, arsenic and iodide have been recommended. In estimating the value of any treatment the tendency of the disease to spontaneous remissions must not be forgotten.

In patients with gangrene, amputation is usually necessary and care should be taken to amputate well above the line of gangrene. By the use of Moskowitz's test the point of election can be determined. The test consists in putting on an Esmarch bandage high upon the affected limb and then removing it. On its removal the blood immediately flows into the well-vascularized portion of the limb which is separated by a line of demarcation from the poorly-vascularized portion. This line of demarcation is the point of election for the amputation.

EMBOLISM

The term embolism is applied to the obstruction of an artery, vein, or lymphatic from the lodgment in its lumen of undissolved foreign matter carried there by the circulation. The mass producing the obstruction is spoken of as an embolus.

¹ Leriche, *La Presse Medicale*, 1922, 30, 1105.

Etiology.—This resolves itself into a consideration of the sources and incidentally the varieties of emboli. It may be well first to consider briefly in a general way the phenomena of embolism. Usually emboli are composed of detached particles of thrombi, and the seat of their lodgment depends on their point of origin. They may be arrested in the systemic arteries, in the pulmonary artery, or in the portal vein. Generally emboli which lodge in the systemic arteries originate in the left side of the heart, in the main arterial trunks, or rarely in the branches of the pulmonary veins. Under some circumstances it is believed that minute systemic emboli may originate in the venous system, passing through the large pulmonary capillaries. Emboli which lodge in the pulmonary artery usually originate either in the systemic veins or in the right side of the heart. Occasionally they originate from non-occluding parietal thrombi of the main branches of the pulmonary artery itself. Emboli which lodge in the portal vein originate in the affluents of that vessel. Ordinarily emboli lodge only in arteries, or in vessels like the portal vein which have peculiarities of distribution like an artery. Ordinarily, too, emboli in the systemic circulation originate only on the left side of the heart, in the larger arteries, or in the pulmonary veins. There are two exceptions to these general rules which must be briefly considered.

Venous emboli have been noted occasionally, usually in veins without valves, and are most common in the subclavian vein, the innominate vein, the axillary vein, the pulmonary veins, the venæ cavæ, the hepatic veins, the cardiac coronary veins, the cerebral sinuses, the mesenteric veins, and the veins of the pampiniform plexus. They are spoken of as “retrograde” emboli, as they are due to the transportation of a thrombus formed elsewhere in the venous system in a direction opposite to the usual course of the blood stream. The cause of these retrograde emboli is probably a backward flow of the venous current due to the sudden temporary stoppage of the return flow of the blood to the heart.

The second exception is the so-called “*paradoxical*” embolus, also spoken of as the “*crossed*” embolus. This name is applied to an embolus lodging in an artery of the systemic circulation which originated in the systemic veins or the right side of the heart and passed through an open foramen ovale. This form is very unusual.

Origin of Emboli.—All emboli are not composed of detached particles of thrombi, for various substances may gain entrance to the circulation and obstruct the bloodvessels. These may be divided into two great groups according to their origin: *endogenous* emboli, which originate within the heart or bloodvessels, and *exogenous* emboli, which have their origin outside of the circulation. Both groups may again be subdivided, according to their nature, into bland or inert emboli, and active emboli, the former being harmless aside from their purely mechanical action, the latter being either infective or composed of living cells or of parasites.

The bland endogenous emboli are usually broken-off particles of bland thrombi, but may consist of detached fragments of calcareous material, of particles of detritus from atheromatous abscesses or ulcers, of pieces of clot from aneurisms or from the heart valves, or of material originating from the destruction of blood corpuscles or of blood parasites such as the malarial plasmodium.

The bland exogenous emboli may be of a solid, liquid, or gaseous nature. Solid emboli originating outside of the vascular system are very rare. There is one remarkable case on record in which a revolver bullet entered the circulation and acted as an embolus. Of the liquid emboli, the most common are fat emboli, usually seen after fractures, but also observed after concussion of the body, inflammation of the subcutaneous fatty tissue, and sometimes after infections. Certain semiliquid or liquid substances introduced subcutaneously for medicinal or cosmetic purposes, such as oil, bismuth salve, mercurial preparations, and paraffin, may also give rise to emboli. Gaseous emboli may be due to the introduction of atmospheric air into the veins during operations or after labor, but in many instances so-called air emboli are due, as Welch has shown, to the production of gases within the circulation by gas-forming bacteria.

The active emboli, like the bland ones, may originate either within or without the circulation. In the first group may be mentioned emboli of leukocytes and emboli originating from infective thrombi. In the second group emboli composed of body cells of various kinds, notably of cells from the bone-marrow, placenta, or liver, are not infrequent, and are sometimes spoken of as autositic emboli. Parasitic emboli are, of course, frequent in bacterial infections, especially in anthrax, glanders, tuberculosis, leprosy, and malignant œdema. The higher forms of vegetable parasites, as the moulds and actinomyces, may also form emboli. Finally, animal parasites, as the larvæ or ova of filariæ, trichinæ, strongyloides, flukes, and teniæ, may obtain entrance to the circulation and produce embolism.

Pathology.—Site of Deposit of Emboli.—It is not to be assumed that all particles free in the circulation succeed in lodging in a vessel. Rarely such particles become entangled in the meshwork formed by the chordæ tendinæ or the columnæ carneæ. Still more rarely large emboli may lodge in the auriculoventricular orifices. It is also to be borne in mind that the caliber of the embolus is often much greater than that of the vessel it obstructs, either because a long, thin embolus becomes folded, thus increasing its diameter, or because an embolus by lodging cross-wise on the partition at the point of division of the vessel (riding embolus) interferes with the circulation of two branches at once.

Emboli free in the blood stream do not lodge indiscriminately in any vessel, but the vessels of certain organs seem especially prone to be plugged. The data are subject to error, for they relate to emboli which have caused distinct lesions, whereas many emboli produce no appreciable gross lesions. Welch believes that the systemic arteries going to the lower extremities receive more emboli than vessels elsewhere. There is a tendency for infective emboli to occur in those places where the circulation is naturally slowest, as in the liver, and also to create lesions in some *locus minoris resistentiæ*. Various lists have been prepared giving the sites of predilection of bland emboli but these frequently do not agree. According to Welch, the vessels most commonly affected are, in the order of frequency, the pulmonary, renal, splenic, cerebral, iliac, and arteries of the lower extremities, axillary and arteries of the

upper extremities, cœliac axis and its hepatic and gastric branches, central artery of the retina, superior mesenteric, inferior mesenteric, abdominal aorta, and coronary of the heart. The vessels most frequently affected are either those in direct line of fire from the commonest origin of emboli, venous thrombi, or those supplying organs whose cells are most easily injured by disturbances in their blood supply. The action of gravity, the weight and size of the embolic mass, and the degree of obliquity with which branches are given off from the main arterial trunk, are the most important of the mechanical factors influencing the lodgment of emboli. Changes in the walls of the arteries, such as roughening from atheroma or narrowing from external pressure, also doubtless play a part in many instances.

Anatomical Characters.—The appearance of emboli varies with their character and age. When seen soon after their lodgment, they are generally easily distinguished from thrombi, but if they have been long in the vessel, so that a secondary thrombus has formed about them, the distinction may be impossible. The fresh embolus is distinguished from the thrombus by its more or less irregular shape, by its lack of adhesiveness or slight adhesiveness to the vessel wall, and by the fact that it may have the appearance of tissue from an old thrombus and that at some point on its surface there is often evidence that it has been detached from a larger mass. The secondary thrombus which usually forms about an embolus causes it to become adherent to the vessel wall, and it then on casual observation appears like an ordinary thrombus. Incision into such a plug may show that the central portion has a much older appearance than the periphery, and may even be calcified, but convincing evidence on this point is often lacking. The most important point in doubtful cases is the detection of a source for an embolus, and unless care is taken this can easily be overlooked. It is impossible in some instances to detect the primary thrombosis, but it is often missed because certain veins which are commonly the seat of thrombi, such as the pelvic veins, are not carefully examined. The condition of the vessel and the clinical history must also be considered in reaching a conclusion.

Effect on the Tissues of the Lodgment of an Embolus.—In certain vessels supplying vital organs, such as the main branches of the pulmonary arteries or of the coronary arteries of the heart, the lodgment of an embolus is usually followed by sudden death. Aside from such special vessels, the changes produced by the lodgment of an embolus depend upon the character of the cells and the circulation of the affected tissue, and upon the character of the embolus. Bland emboli produce merely mechanical effects; active emboli produce in addition chemical and sometimes vital changes.

The effect of the lodgment of bland emboli in the vessels of certain organs and tissues with an extensive and freely anastomosing blood supply, and cells which bear well temporary interference with their nourishment, may be quite inappreciable. Thus emboli of the vessels of the liver, the thyroid, the bones, the urinary bladder, the female genital organs, and the more vascular portions of the skin, result as a rule, in a temporary anemia quickly followed by the formation of a collateral circulation.

Bland emboli in tissues whose circulation is anatomically terminal, or is insufficient to supply blood by collaterals to cells easily succumbing to the effects of anemia, result in necrosis. The type of necrosis produced varies according to the character of the structure affected, and its relations to the surrounding tissue. If the part whose circulation is cut off is segregated from the rest of the tissues, as occurs after embolism of the main artery of an extremity, the resulting process is known as gangrene or mortification. If the affected tissue is a small segment of an organ, and is surrounded by normal tissue from which lymph can flow into it, the result will be either an area of softening, as occurs in the central nervous system, or, if large quantities of coagulable material are absorbed by the necrotic cells, coagulation necrosis in the form known as an infarct. In certain structures, as the kidney, spleen, brain, intestine, and retina, infarction almost invariably takes place. In others, perhaps on account of individual peculiarities in the circulation, it does not always occur. Thus bland emboli in the lungs do not usually produce infarcts. Bland emboli of the larger cerebral arteries, on account of the circle of Willis, often produce but little effect. Embolism of the main vessels of the extremities, and even of the aorta itself, may not result in necrosis.

When infarctions occur their appearance is not always the same owing to individual peculiarities in the cells or tissues of certain organs. In general, *infarcts* have a conical shape with the base of the cone toward the periphery of the organ, this being due to the fact that they correspond to the distribution of the branches of the particular arterial trunk which has been plugged. Their consistency varies somewhat with the character of the organ, being not quite so firm in a loose-meshed organ with chances for expansion as in a compact one enclosed in an unyielding capsule. The main variation, however, lies in the color, which may be red (hemorrhagic) or white (anemic). Some describe mixed infarcts, and in the kidney, where the distribution of the vessels in the medulla is different from that in the cortex, a white infarct with a red apex may occur if the infarcted area is partly included in the medullary zone. The factor which makes the difference between the red and the white infarct is the presence in the infarcted area of red blood corpuscles, and the character of the cells of the affected organ, or sometimes other peculiarities of structure, determine whether red blood cells shall be present in numbers. In the kidney soon after the blood supply is shut off from the affected part, the sensitive cells die and absorb serum from the small amount of blood carried in by the scant collaterals. As a result the cells swell rapidly, compress the cortical vessels, and prevent any marked influx of blood. We therefore usually get white infarcts in the kidney. Very much the same thing occurs in the brain, whose cells are even more sensitive to interference with their blood supply than those of the kidney. Here instead of a white infarct we get an area of white softening. In the spleen, on the other hand, the interference with the blood supply irritates the muscle fibres in the capsule and trabeculae, and causes them to contract, forcing out the blood. After a certain period, perhaps some days, the muscle relaxes, but by this time changes

in the walls of the vessels have occurred. They are no longer able to retain the blood, which escapes into the affected area and swamps it with serum and corpuscles, resulting in stasis and finally necrosis. In the lung the element of infection comes into play, the bacterial toxins producing changes in the vessel walls which allow the passage of the blood into the alveoli. Here also stasis and necrosis result. Microscopically the tissue in infarcted areas has the usual appearance of necrotic tissue, except that usually the structure of the affected organ is at first to be made out perfectly. As the infarct grows older, signs of reaction on the part of the surrounding tissue, the wandering in of leukocytes, and proliferation of the connective-tissue cells, become apparent.

In a good many instances infarction occurs only during the terminal stages, but sometimes patients survive for a long period after it has occurred. In such patients infarctions undergo a process of organization similar to that already described under Thrombosis, and the infarct is replaced by a cone-shaped patch of scar tissue very much smaller than the original infarct. Such scars are common enough in the kidneys, are less common in the spleen, and are rare in the lungs, as pulmonary infarcts are almost always forerunners of death. Certain bland emboli, such as air, fat, and parenchyma cell emboli, produce special effects.

The effect of the lodgment of the so-called active emboli depends on their nature. The most important of them are the infective emboli, emboli of tumor cells, and parasitic emboli.

Infective emboli produce the same mechanical effects as bland emboli, and in addition changes due to the action of the contained bacteria and their toxins. As in other infections two factors are to be considered; the virulence of the infective agent, and the resistance of the individual. Inasmuch as the virulence of the bacteria in infective emboli may be slight, and the resistance of the individual to infection may be great, we find that many infected emboli produce only mechanical effects. Not only the general resistance, but also variations in the local resistance are to be reckoned with. Such variations differ to some extent in individuals of the same species, and to a more marked extent in individuals of different species. Where the individual resistance is lowered or the bacteria in the emboli possess a high-grade of virulence, we see, besides the ordinary mechanical effects, the production of hemorrhages, of extensive necrosis, of metastatic abscesses in the tissues in which the emboli lodge, and, if putrefactive bacteria are present, of areas of gangrene.

Embolio Aneurisms.—One of the rarer complications of embolism is the production of embolic or mycotic aneurisms. Such aneurisms usually occur as a result of the direct action of pyogenic bacteria contained in infected emboli on the walls of the affected artery. The infection causes a partial destruction of the coats of the vessel and a consequent weakening. Rarely the traumatic action of sharp emboli of calcific material may lead to aneurism formation, but this form is very unusual. These aneurisms may develop upon any vessel, but most often in those vessels which are lacking in support from surrounding tissue. They are more common for this reason in such arteries as the mesenteric, the more superficial peripheral arteries, and the cerebral arteries. The aneurisms are usually

associated with general sepsis, especially sepsis with endocarditis. They are especially likely to occur in the type of subacute endocarditis generally due to the *Streptococcus viridans*.

Of the other varieties of active emboli, those of tumor cells and of animal parasites deserve brief mention. *Tumor cells* may gain entrance to the circulation either by direct growth into the bloodvessels or indirectly by way of the lymphatics and the right heart. In some types of tumor, notably certain neoplasms of the testicle and kidney, it is not unusual for extensive growths to penetrate the veins, from which they may extend even to the cavities of the heart. Large masses may be detached from such tumor thrombi and may cause fatal embolism of the pulmonary arteries. Ordinarily, however, tumor emboli are small, so small that they are more apt to lodge in the capillaries than elsewhere. Those originating in the general circulation usually gain entrance to the veins and naturally tend to be arrested in the lungs, although probably a fair percentage of them pass the large pulmonary capillaries and get into the general arterial circulation. Paradoxical emboli of tumor cells are not very uncommon. In tumors of the abdomen arising in organs whose vessels drain into the portal system the liver is naturally the seat of the most extensive deposits of neoplastic emboli. A good many tumor-cell emboli die, but in many instances they cause metastases. Aside from the lungs and liver, the bones, the kidneys, and the skin seem especially liable to be the seat of such secondary embolic nodules.

Certain *animal parasites* or their ova may act as emboli. Of the smaller ones, the malarial parasite is the most common. In the pernicious type of malaria, the capillaries of the brain are often plugged with parasites. Occasionally they accumulate in the kidney vessels, as shown by Ewing, and the writer saw one case in which the smaller pulmonary vessels appeared as if injected with them. Amœbæ have been observed in the bloodvessels, and some amœbic abscesses of the liver probably originate from emboli of amœbæ in the branches of the portal vessels. Emboli of the larger parasites or their ova are more common in the lower animals than in man, although the *Trichinella spiralis* during certain stage of development occupies the vessels, as evidenced by the œdema which accompanies trichiniasis. Echinococci occasionally act as emboli, and in the lungs are stated to produce special symptoms.¹

Symptoms.—The symptoms produced by the lodgment of an embolus, vary according to the character of the obstruction and the function and structure of the tissue involved. Certain symptoms of a local and general character common to all varieties of emboli may be briefly considered here. *Pain* is an almost constant accompaniment of embolism of the peripheral vessels, but is less common in embolism of visceral vessels. In many instances it is very abrupt in onset, and the patient may experience the sensation of a sudden painful blow. In some cases it is not very marked, but it may be intense. It is doubtless due at the onset to the mechanical action of the embolus on the nerves of the affected vessel from impact and stretching, but later in infective emboli the direct

¹ Garnier and Jomier, *Presse méd.*, 1905, 1, 369.

action of the bacteria or toxins on the vessel wall plays a part. In both bland and infective emboli the anemia of the area supplied by the embolized vessel also accounts for some of the pain, as it causes irritation of the sensory nerves. Pain of a secondary character, due to the production of inflammation in the involved tissues, occurs in connection with septic emboli. Evidences of interference with the circulation are not visible except in emboli of the vessels supplying the extremities or surface of the body. They may appear indirectly, however, in pulmonary embolism in the form of hemoptysis, in mesenteric embolism as hemorrhagic diarrhœa, and in embolism of the renal artery as hematuria. Evidences of impairment of function in visceral embolism are often slight or absent, except in the case of organs such as the central nervous system, in which definite functions are associated with sharply localized areas. Embolism of the vessels of other internal viscera may be accompanied by impaired function if large areas are thrown out of action. If only a small area is affected the lesion is compensated for by the uninvolved portions of the organ, or in the case of paired organs, by the normal one. General symptoms such as chills, fever, headache, and rapid heart's action, are not usually marked except in connection with septic emboli, and are due to the sepsis. Slight fever and acceleration of the pulse may occur as a result of bland emboli.

Air Embolism.—The association of sudden death with the entrance of atmospheric air into the veins has long been known. As a rule it only occurs when veins of a fair size and situated near the heart are opened. It is therefore especially liable to occur in connection with operations on the neck, not only because the veins of the neck are near the heart, but also on account of the fact that these vessels are held open by their relation to the fascia, and because the aspiration of the thorax acts forcibly here and tends to suck in relatively large quantities of air in a short time. Air embolism has also been described in connection with wounds of other superficial veins, usually of the upper extremities or the head, and as a complication of operations on the uterus during the puerperium, or even of simple intra-uterine douching. Rarely air embolism has been reported as a complication of gastric ulcer.

A large number of supposed cases of air embolism will not stand critical inspection. Welch and Flexner¹ pointed this out in an article on the *Bacillus aërogenes capsulatus*, remarking "that of the considerable number of reported cases of suspected entrance of air into the bloodvessels, none seem to have been previously the subject of bacteriological study." Cases of supposed air embolism after labor or in connection with diseases of the gastro-intestinal tract must be scrutinized with special care, for in both these situations infection with the gas bacillus has been shown to be not infrequent.

Making due allowance for infection with gas-forming bacteria, there remains a certain number of cases in which no doubt exists that the entrance of air into the veins caused death. Experimental work on the lower animals has shown that it is possible to cause death in this way,

¹ *Jour. Exp. Med.*, 1896, **1**, 5.

although in dogs, the animals usually employed, large amounts of air are required, and the chances of producing a fatal result are greater the nearer the heart the air is introduced. The cause of death, according to Wolf,¹ is nearly always pulmonary embolism, although occasionally coronary or cerebral emboli cause the fatal result. As a rule the air does not penetrate beyond the pulmonary capillaries, and Wolf seems inclined to throw out of the category of air embolism cases in which air was found in any quantity in the general circulation.

The *symptoms* of air embolism in well-marked cases are striking and easily recognizable. Usually during the course of an operation on the neck the surgeon is suddenly startled by the sound produced by the entrance of air into a severed vein. This is described by Koenig as a "lapping" murmur. In some instances the patient dies with lightning-like rapidity; in others death is preceded by signs of apprehension, dyspnoea, cyanosis, trembling, dilatation of the pupils, syncope, and convulsions. A distinct churning sound, which Wolf believes is due to the mixture of air and blood being pressed behind the columnæ carneæ or being forced through the pulmonary valves, may be heard in many cases on auscultating over the heart. The symptoms last but a few seconds, and most patients die, although recoveries are recorded. The cases of E. Janeway and Hun, in which cerebral symptoms followed the introduction of peroxide of hydrogen into the thoracic and abdominal cavities respectively, should possibly be classed with air embolism.

Fat Embolism.²—Most commonly met with after fractures of the long bones, emboli of fat have also been encountered after orthopedic operations, especially brisement forcé, after ordinary surgical operations and operations on the bones, after contusion or laceration of the subcutaneous fatty tissue, and in association with infections with fatty degeneration of the organs, with atheroma of the arteries, and with diabetes mellitus. The complication has also followed the subcutaneous introduction of oil for purposes of nutrition. The view generally held regarding the origin of fat emboli associated with fractures has been that they originate as a direct result of the entrance of fat into the vessels at the point of local injury to the bone. Ribbert³ claims that the amount of fat found in the lungs is too great to have originated in this way, and he explains the lesion as due to the escape of fat from the general jarring of the bones. The fat emboli are found in some patients merely in the lungs; in others, after an interval of one or more days, some of the emboli pass on and lodge, especially in the muscle of the right side of the heart and in the brain. In these situations they produce areas of hemorrhage and fatty degeneration probably sufficient to account for the cardiac and cerebral symptoms. The emboli also lodge in the spleen and kidneys. Here they do not produce any appreciable symptoms, though fat is commonly excreted with the urine in the case of kidney involvement.

Symptoms of fat embolism are in most instances lacking, although in severe cases sudden death may ensue. In a certain number of patients

¹ *Virchow's Archiv*, 1903, vol. 174.

² Connell, *Jour. Am. Med. Assn.*, 1905, 44, 612.

³ *Deutsch. med. Wchnschr.*, June 28, 1900.

symptoms definite enough to allow of a diagnosis occur. These may appear immediately after the injury, but are usually delayed from six hours to fifteen days. Where immediate symptoms appear they are pulmonary and take the form of a rapidly fatal asphyxia. Commonly the patient, who has perhaps reacted from the shock of the fracture or operation, is noticed to be breathing more rapidly than normal, appears anxious, may be restless, or on the other hand somnolent, and may complain of pain in the side. Sometimes hemoptysis is present. Examination shows the appearances often ascribed to shock; pallor, perhaps cyanosis, a cold skin and a rather feeble, rapid, and irregular pulse, and probably slight elevation of the temperature. In severe cases contracted pupils, diminished reflexes, Cheyne-Stokes respiration, convulsions, and coma may occur, and death may close the scene. Localized signs of consolidation of the lung with a few rales may be present. They are most apt to be heard posteriorly over the bases of the lungs. The presence of fat in the urine is an important diagnostic sign, and fat may be found in the sputum also. In a patient seen with my colleague, Dr. Sanford, there was a slight leukocytosis, 14 per cent. of the cells being neutrophilic myelocytes.

The *prognosis* is uncertain. The mortality from fat embolism after fractures is probably not over 1.5 per cent. The diagnosis is not necessarily difficult. It may be confused with shock or with ordinary embolism, but shock occurs much sooner after the operation or injury than does fat embolism, and ordinary emboli are a late complication. The presence of fat in the urine is of diagnostic value, but may occur without symptoms of fat embolism. If associated with localized lung signs, slight fever, rapid pulse, and respiration, and mental unrest or somnolence, these symptoms appearing from six to seventy-two hours after a fracture, the probabilities are in favor of fat embolism. In operative cases the differentiation from the effects of anesthetics may be difficult, and sepsis may be suspected in patients with a good deal of fever.

Cell Emboli.—Apart from emboli of tumor cells, there have been described emboli composed of the cells of normal organs or tissues, and more recently emboli of phagocytic cells associated with infectious diseases. Of the normal cells, those of the liver, placenta, and the bone-marrow are the ones most commonly found as emboli.

After injuries, not only cells but actual fragments of liver tissue and bone-marrow may be transported, and even whole chorionic villi have gained access to the circulation. In typhoid fever large phagocytic cells may gain entrance to the portal circulation, as the studies of Mallory¹ show, and MacCallum² has demonstrated that the same cells may enter the lungs through the thoracic duct. Most cell emboli lodge in the pulmonary vessels, but a few reach the general circulation through an open foramen ovale. These emboli are not usually large enough to cause lesions of an extent sufficient to produce clinical symptoms, though occasionally they may cause quite extensive pulmonary infarction.

Mercurial Emboli.—The introduction of the use of insoluble mercurial salts by the hypodermic route was soon followed by evidence that

¹ *Jour. Exp. Med.*, 1898, **3**, 611.

² *American Medicine*, March 21, 1903.

embolism at times resulted. The accident occurs after the use of the salicylate of mercury, of gray oil, of calomel, and of other insoluble preparations, especially when paraffin is used as a vehicle. The frequency of the complication is hard to judge but it probably occurs in about 1 per cent. of patients so treated.

The *symptoms* depend upon the point of lodgment in the lungs, the emboli which lodge peripherally causing involvement of the pleura and therefore pain. In such cases the characteristic symptoms are the sudden onset, soon after the injection, of paroxysmal cough, with lancinating pain in the side, sometimes chilly sensations, and usually fever. In some instances no symptoms appear for at least twenty-four hours after the injection. Fever may be absent, and, if the emboli are deep-seated, pain is not usually present. The physical signs of a patch of consolidation associated with rales may sometimes be detected. The *diagnosis* is obviously simple, although it must be borne in mind that in cases of fresh luetic infection fever, chilly sensations, and anorexia may follow the injection of mercury without the presence of lung emboli. The prognosis is so uniformly good that some syphilographers take it for granted that the complication will occur and consider it no obstacle to the hypodermic use of mercury. According to Heidensfeld, embolism may be avoided by using lanolin as a vehicle for the mercury. Similar emboli may follow the use of bismuth paste in sinuses.

Paraffin Emboli.—The subcutaneous use of paraffin for cosmetic purposes has been followed in several instances by paraffin embolism of the central artery of the retina. The complication usually ensues immediately after the injection of the paraffin. The patient may show marked symptoms of collapse and sudden loss of sight on one side. The loss of vision is usually permanent. According to Stein¹ the complication may be avoided by using only soft paraffin, injecting it only when it has a pasty consistency, and never using more than 3 cc. at a sitting.

Embolism of Special Arteries.—Embolism of the Pulmonary Artery.—This is the most frequent form of embolism and is much more common than thrombosis of this vessel. Pulmonary emboli occur most frequently in connection with heart disease, usually originating from thrombi in the right side of the heart, and in connection with certain forms of peripheral venous thrombosis, especially the puerperal type and some other varieties mentioned in the article on thrombosis. Occasionally pulmonary embolism arises from the detachment of portions of parietal thrombi in the larger branches of the vessel itself. The symptoms produced by the lodgment of an embolus in a branch of the pulmonary artery depend mainly upon the size of the vessel which is obstructed. Blocking of the trunk or of one of the main branches usually results in sudden death. This may occur at once, but is often delayed a few seconds, during which time the patient is almost apnoëic, is gasping for breath, deadly pale, and practically pulseless. The sufferer may cry out at the time of lodgment of the embolus, and may grasp the precordial region with an expression of great anguish. In a few rare instances occlusion of the main trunk has occurred without causing immediate death or marked changes in the lungs.

¹ *Deutsch. med. Wchnschr.*, 1903, vol. 39, Nrs. 36-37.

When a medium-sized branch is plugged, or when an embolus lodges in a large branch, but does not completely occlude the lumen of the vessel, the patient may survive for hours or days, or may even recover completely. The most prominent symptoms in these patients are the rapid respiration and the marked dyspnoea, both of which in the early stages are out of all proportion to the signs of pulmonary involvement. The dyspnoea and the intense sensation of oppression in the chest which accompanies it, recall cardiac dyspnoea, but the rapidity of onset of the symptoms in embolism and their great intensity are points of distinction. Lancinating pain in the chest may be present in patients with embolism of this type, but it is unusual. It may be absent at first, but present later in patients who survive long enough for the development of pleural involvement. The physical signs vary in such patients at different periods. At first the patient is pale, later often markedly cyanotic, extremely restless and anxious looking. A marked effect on the circulation is apparent from the first. The heart is weak, perhaps irregular, and the pulse is small, feeble, and very compressible. Systolic and diastolic murmurs at the base of the heart have occasionally been described. Physical signs in the lungs are at first absent. After twenty-four hours, if the patient survives that long, there may be impaired resonance over a part or the whole of one lobe, usually a lower lobe. This is generally accompanied by feeble breath sounds and a few fine, moist rales which later may become much more numerous. At the time the definite lung signs develop the patient may have a profuse, frothy, or bloody expectoration, but this usually disappears in a few days. There is often some fever, although this is not as a rule high. The mind is usually clear, although convulsions and coma may precede death in fatal cases. Recovery may occur in patients with severe symptoms. Leopold reports the case of a patient who recovered after three severe attacks.

Obstruction of the smaller branches of the pulmonary artery when associated with chronic passive congestion or pleural effusion, may lead to the formation of a hemorrhagic infarct. Such infarcts occur in nearly 50 per cent. of all cases on the right side at the base of the lung.

Symptoms of pulmonary infarction are not always present. In some instances the lesion is entirely latent. In other cases the symptoms which accompany the embolism of a large pulmonary vessel are present in a modified form. There is a sudden attack of pain in the side, usually the right, with a rigor or chilly sensations, an increase in dyspnoea, rise in the temperature, and perhaps bloody, or, at any rate, blood-streaked expectoration. True hemoptysis in the sense of the expectoration of pure blood is rare, but blood-streaked sputum is not uncommon, and should always suggest infarction in a patient with heart disease in the stage of broken compensation. Physical signs can be detected in a great many patients with pulmonary infarction, as the lesion is most common at the bases of the lungs and because most infarcts involve the periphery of the organ. The detection of certain signs, such as definite dulness or changes in the fremitus, depends on the size and situation of the infarct. On palpation, as a rule, marked signs are absent, although in case of a large infarct superficially situated, the fremitus is generally

decreased. One or more circumscribed areas of dulness may often be made out. The dull note not infrequently has a tympanitic quality, this being due at times to the collapsed condition of the lung about the infarct and at times to the transmission of resonance from a large bronchus through the consolidated lung. Auscultation during the early stages may reveal fine crepitant rales, although these do not usually last long. The breath sounds over the area of consolidation may be feeble or almost lacking or, if the area is in contact with a fair-sized bronchus, there may be marked bronchial breathing. As a result of atelectasis of areas about the infarct, crackling rales may be heard. A pleural rub may be heard when the infarct is superficial.

The *diagnosis* of pulmonary embolism involving the larger vessels is based on the sudden onset of intense pulmonary symptoms in a patient suffering from some disease which is commonly associated with venous or cardiac thrombosis. The more prominent of these diseases and the frequency of their association with embolism have been noted in the article on Thrombosis. In women the puerperal state and chlorosis should always be regarded with suspicion, and in both sexes patients should be watched during and after the infectious and cachectic diseases, local diseases of the veins, cardiac disease, and abdominal operations. The source of the emboli in many cases is obscure.

The *prognosis* in pulmonary embolism is always grave. In the puerperal form 60 per cent. of the patients die, according to Richter. Embolism in chlorosis has a prognosis even graver than this. Recovery from embolism of the larger branches of the pulmonary artery is very rare, although it does occur. Recovery after smaller emboli with infarction is also uncommon. According to Romberg, of 43 patients with heart disease and signs of lung infarction observed in his clinic, 36 died. The prognosis depends not only upon the size and character of the embolus, but also upon the general condition of the patient.

Embolism of the Splenic Artery; Splenic Infarction.—The appearance of an infarct in the spleen is often unaccompanied by characteristic symptoms or signs. In some instances the diagnosis can be made. The most important signs are sudden pain in the splenic region, with enlargement of the spleen. Sometimes the onset is accompanied by a definite rigor. Vomiting is not uncommon, according to Leube. Pain is not always present. The swelling of the spleen is not usually very marked, but the organ is generally palpable, and there may be a localized point of special tenderness with an overlying friction rub due to localized peritonitis. Fever is not marked unless the infarct is a septic one, in which case there may be a high fever a few days after the onset of signs, and chills may occur. When suppuration follows a septic embolus, marked signs of local peritonitis may occur and there may be general peritonitis from rupture of the purulent focus. Even with bland emboli there are sometimes very marked signs of local peritonitis. The presence of a source for embolism will, of course, have great weight in the diagnosis.

Renal Infarction.—This is often latent but in some instances definite evidences of kidney involvement are present. The most important of these are changes in the urine and pain and tenderness in the kidney

region. In bilateral infarction of the kidney there may be complete suppression of urine, but this never occurs in unilateral infarction. As a rule there is some diminution in the quantity of urine, with the presence of large amounts of albumin and perhaps some blood. Schmidt states that hematuria is quite uncommon. It is perhaps overlooked in some instances. The absence of casts or marked sediment may be a striking feature of albuminuria from embolism, and is probably due to the fact that no urine is secreted in the infarcted area and nothing is therefore washed out of it. The occurrence of pain, sometimes intense, is not infrequent in connection with kidney infarcts. At times it is described as burning or as a sensation of pressure. Its very sudden onset is often suggestive. It is situated as a rule in the kidney region, radiates but little, and is never referred to the external genitals or to the shoulder-blades. It is more constant than the pain of ureteral calculi. The pain is associated with marked tenderness in the kidney region and may be increased by coughing, deep breathing, and vomiting.

The *symptoms* of kidney infarct may be confounded with those of Dietl's crisis from movable kidney, with pain accompanying the sudden congestion of a tumor of the kidney, or with the pain of an acute exacerbation of a chronic nephritis. The pain in the infarct is usually more severe than that accompanying an exacerbation of an old nephritis, and is more marked on pressure. The onset of a Dietl's crisis often follows exercise, while the pain of infarct often appears while the patient is in bed. Other conditions, such as gall-stone colic, lead colic, and ureteral colic might cause confusion but the differential points readily suggest themselves. Evidence of some source for an embolus is very important in making a diagnosis.

Embolism of the Mesenteric Arteries.—Embolism of the mesenteric arteries has been considered under the head of Thrombosis.

Embolism and Thrombosis of the Aorta.—Embolism and thrombosis of the thoracic aorta are extremely rare for with the great force of the blood stream through this vessel it is only very exceptionally that a thrombus can form or an embolus gain lodgment. Complete obstruction of the thoracic aorta is followed by death, usually very suddenly, at latest after a few hours. Incomplete obstruction either produces no appreciable symptoms, or, if marked, leads to the same changes which characterize obstruction of the abdominal aorta together with, in some instances, signs of blocking of the arteries of the upper extremity.

Embolism and thrombosis of the abdominal aorta are best considered together, for although there exist instances in which the gradual progress of the disease seemed to show that thrombosis was the lesion, it is often impossible to determine whether the obstruction is due to a thrombus or an embolus. Thrombosis of the aorta may suddenly give rise to very acute symptoms and embolism may rarely occur without signs of sudden onset. The thrombi occupy as a rule that portion of the abdominal aorta which lies below the point of origin of the main branches, *i. e.*, below the origin of the mesenteric arteries. This part of the vessel is considerably narrower than the rest of the main trunk and is the section in which, under conditions of enfeebled circulation, the best chances for

the formation of a thrombus or the lodgment of an embolus are to be found. Most cases of aortic thrombosis are associated with disease of the vessel wall, usually arteriosclerosis, while of the cases which appear to be embolic—and these constitute a large majority—the greatest number are associated with mitral stenosis. When this latter lesion is present there is frequently evidence that thrombosis has been present somewhere in the left side of the heart, and while this is sometimes lacking, aortic emboli originate in most instances in this situation. In other cases external pressure plays a part, or the embolus is furnished by a thrombosed aneurism of the thoracic aorta.

The *symptoms* of obstruction of the aorta vary. In some patients with aortic thrombosis the symptoms are obscure and cannot be definitely referred to a lesion of the aorta. In patients with definite symptoms, these may be gradual or sudden in onset. When the onset is gradual it is believed by some observers that the patient may survive two, three, or even four years after the appearance of the first symptoms. Mazoux lays stress on the importance of intermittent claudication as an early sign of the gradually progressing form of thrombosis of the abdominal aorta.¹ As the disease progresses this symptom becomes more and more marked and may be associated with severe pain in the lumbar region radiating to the limbs. There may be sensations of numbness and formication in the feet. Finally a paraplegia of the lower extremities develops, usually followed by gangrene of parts of one or both lower limbs. The character of the paraplegia is not well described in many of the reports. Usually it seems to be incomplete, limited movements of the limbs being possible. The state of the reflexes varies; in some patients they are abolished; in others, the paralysis being spastic, they are presumably increased. The occurrence of gangrene is preceded first by coldness and pallor, later by cyanosis of the extremities, and in some cases by chronic ulcerations. Usually severe pain in the legs is an accompaniment of the gangrene. The extent of the mortification varies, this probably depending in part on the completeness of the obstruction of the aorta, in part on the number and distribution of collateral vessels. Œdema is not marked, as a rule, and may be absent.

In patients in whom the onset of aortic obstruction is acute—and these constitute the majority—*pain* is usually the most prominent of the early symptoms. It is generally intense and referred to the lower extremities. The patient may be struck as by a shock and fall to the ground in intense anguish. In most instances there is a markedly anxious expression. Occasionally pain is absent, and, on the other hand, it sometimes occurs in paroxysms separated from one another by periods of several days. Other symptoms are very variable. Usually there is pallor of the skin of the extremities, followed by lividity, diminution of sensation, paresis and finally paralysis of the muscles, and gangrene. The pulsation in the vessels of the legs is very feeble or entirely absent. General symptoms may occur. The intense pain may cause marked psychic disturbances. There is sometimes a gradual rise in the temperature. The pulse usually

¹ Mazoux, *Thrombosé de l'Aorte*, Thèse de Paris, 1905.

becomes distinctly weaker and more rapid than it was before the onset of the symptoms. If the renal vessels are involved symptoms of renal infarction or even total suppression of urine may occur. Involvement of the mesenteric arteries will produce the intestinal symptoms already described under Mesenteric Thrombosis. Pain in the lower abdomen and tenderness over the aorta are not infrequently present.

In the *diagnosis* of a typical case there is hardly any doubt. Some of the more chronic cases might, at some stages, suggest Raynaud's disease, but the fact that only the lower extremities are affected, the progressive character of the lesion, and the lack of arterial pulsation should rule this out. In patients without much pain an acute myelitis might be suggested, but the pallor of the skin, the cold lower extremities, and the absence of pulsation in the vessels of the legs should prevent this mistake.

The *prognosis* is exceedingly grave. Very few patients have recovered. Death may take place the same day that the symptoms appear; usually the end comes within fifteen days from the onset. Some patients, however, live several weeks, and a few survive several years after the symptoms first manifest themselves.

Embolism and Thrombosis of the Subclavian Artery.—Embolism of the large branches of the arch of the aorta is extremely rare, most instances of obstruction being due to thrombosis.

The *symptoms* of obstruction of the subclavian artery are very variable, and, considering the size and importance of the vessel, the lack of striking symptoms is often the most marked feature. There may be paroxysmal neuralgic pain in the neck and shoulder on the affected side, and this may be markedly influenced by changes in the weather. Occasionally there is distinct weakness of the arm which may almost amount to paralysis. The objective signs are the result of the obstruction to the circulation. The pulsation in the radial artery on the thrombosed side is in some instances not influenced in the least; in other patients the *pulsus differens* may occur. The pulsation in the carotid artery on the affected side is usually unimpaired, although it may be a little weaker than normal. In some patients changes in the skin are present in the form of great dryness, or sometimes a patchy oedema. There may be a wasting of the muscles of the arm. Gangrene is usually absent, and its presence is stated to indicate that the process is a luetic one.

The *diagnosis* can only be positively made during life by palpation of the arteries on each side with the demonstration of lack of pulsation in one of them. In a few instances a thrombus may extend into the axillary or brachial arteries and the vessels may be felt as firm cords.

Embolism and Thrombosis of the Carotid Artery.—Embolism of the common carotid artery is very unusual, the internal carotid being much more frequently affected. Thrombosis is more common than embolism, and is usually associated with arteriosclerotic changes in the vessel wall. Occlusion of the carotid is of interest on account of its relation to the cerebral blood supply. As has been abundantly proved by ligature of the vessel, the effect of obstruction on the cerebral circulation is usually slight, not infrequently entirely negative. The anastomoses with neighboring vessels are extensive, the most important in the case of the external

carotid being the branches from the carotid of the other side; in the case of the internal carotid, the vertebral arteries and the circle of Willis. In some instances the collaterals seem to be poorly developed or unable to supply the increased demands, and symptoms of cerebral anemia and softening occur. The patient may complain of giddiness, and there may be convulsions, stupor, coma, and eventually hemiplegia on the side opposite the lesion. In some patients there is paralysis of one side of the face only or of one limb. Aphasia may follow thrombosis of the left carotid artery. The diagnosis may sometimes be made during life by detecting the thrombosed vessel as a sensitive cord. The rapidity with which occlusion occurs influences the symptoms, and embolism is, for this reason, more apt to produce serious symptoms than thrombosis.

Embolism and Thrombosis of the Arteries of the Extremities.—A distinction between embolism and thrombosis of the arteries of the extremities is sometimes possible from the fact that in arterial thrombosis the onset of the symptoms is often gradual. It has been shown, however, that the onset of symptoms in thrombosis is frequently just as abrupt.

The *subjective symptoms* of obstruction of the peripheral arteries are quite similar to those of venous obstruction. They depend largely on the number of anastomosing vessels and the rapidity with which a collateral circulation is established. The result of plugging of peripheral arteries is less marked in the upper extremities where the collaterals are numerous, but depends also on the condition of the circulation in general and upon the presence or absence of vascular disease. Naturally the obstruction of an artery will produce quite different effects in a young, relatively vigorous individual with sound arteries and in an old feeble person with diseased vessels. Pain is practically always present, usually sudden in onset, and often extremely severe. It is due to the stretching of the vessel, and in embolism also to the impact of the embolus. As a rule it is associated with hypesthesia or complete anesthesia in the part rendered anemic, and disturbances of motion ranging from paresis to complete paralysis. The affected limb is usually at first pale and cold, and although œdema is often present, it is generally slight and not to be compared in degree to the œdema of venous thrombosis. Palpation of the affected artery below the point of embolism demonstrates a lack of pulsation. Tenderness of the vessel is also usually present. As time goes on, if the collateral circulation is not established, the pallor of the limb changes to cyanosis or a mottled appearance, and finally gangrene occurs. If the embolus is infective we see, besides these changes due to mechanical obstruction, perivascular suppuration and perhaps the formation of an embolic aneurism.

The differentiation of arterial thrombosis from arterial embolism is often impossible and not of any particular importance. The differentiation of embolism from venous thrombosis is usually easy. Pain is common to both, but in embolism lack of marked œdema, the loss of arterial pulsation, the more marked sensory symptoms and paralysis, and above all the gangrene, usually leave little room for error. Besides this, a source for the embolus can frequently but not invariably be made out.

So far as the loss of a limb is concerned, the *prognosis* depends upon

the artery affected and the general condition of the patient. Plugging of the arteries of the upper extremity is less serious than obstruction of the vessels of the legs. Thrombosis or embolism of the femoral or popliteal arteries almost invariably results in gangrene, whereas even the subclavian may be obstructed without gangrene of the hand or arm. Gangrene is much more apt to occur in patients with an enfeebled circulation and preëxisting arterial disease. If a patient is already enfeebled and shows evidences of embolism elsewhere, the obstruction of a peripheral artery may be the direct cause of death. Naturally the arterial obstruction resulting from chronic heart disease with failing compensation is much more serious than that in the infectious diseases.

Obstruction of the Hepatic Vessels; Hepatic Infarction.—The types of thrombosis of the hepatic vessels associated with clinical symptoms have been discussed. Brief mention must be made of the infarcts of the liver which, however, are not known to be associated with distinct clinical features and are of pathological significance only. Two forms of liver infarction are to be recognized; the white infarct, usually due to obstruction of a branch of the hepatic vein, but occasionally resulting from portal obstruction or rupture of the liver, and the so-called “atrophic red infarct” of Zahn, which occurs in certain cases of thrombosis or embolism of the branches of the portal vein.

Embolism and Thrombosis of the Coronary Arteries of the Heart.—Thrombosis of the coronary vessels is much more common than embolism. In view of the situation of the origins of the coronary arteries, their size, and the frequency with which degenerative changes attack their walls, it would seem that the chances in favor of thrombosis are much greater than those in favor of embolism. A few observers, Romberg for example, state that the large and medium-sized coronary vessels are most frequently obstructed by emboli, but the mass of pathological evidence contradicts this. When thrombosis does occur, it is usually associated with arteriosclerosis, and considering the frequency with which this occurs, it is strange that thrombosis is not more common. Embolism of the coronaries is usually associated with general sepsis and endocarditis, and the emboli are therefore usually infective. Bland emboli in the coronaries have been described in a few instances.

Whether the stoppage of the coronary artery is due to a thrombus or an embolus, the result is much the same, and depends partly on the size and distribution of the occluded branch, partly perhaps on the presence or absence of preceding disease of the vessel and partly on individual peculiarities in the circulation. Stoppage of the main branch of the coronary artery results in most instances in sudden death, though this is not invariably the result. There may, in fact, be obstruction of the two main branches, without any marked cardiac symptoms during life. Such instances are due to individual peculiarities in the circulation, and in most patients a fatal issue may be expected from a few seconds to a few hours after the obstruction has occurred.

When obstruction of the coronary artery is not immediately fatal it leads to changes in the heart muscle. There may be merely fatty degeneration of the area of muscle supplied by the occluded vessel, but usually

an infarction results. The occasional exceptions only go to prove the rule that the coronary vessels are terminal vessels, at any rate after they have penetrated the musculature. The common site of the larger infarcts is the anterior surface of the apical one-third of the left ventricle and the septum near the apex, and this because the descending branch of the coronary artery is the one most frequently involved. Occasionally infarcts occupy the wall of the ventricle near its base, and still more rarely the right ventricle is involved. Cardiac infarcts are often irregular in shape, and generally have a characteristic yellowish color and a peculiar dry consistency. They are often hemorrhagic about the edges. On their ventricular surface they are usually covered by a mural thrombus, while their pericardial surface is generally the site of a pericardial exudate which may later organize, obliterating the pericardial cavity over the affected area and doubtless affording some protection against rupture and aneurism formation. If the obstruction and resulting infarction are not soon followed by the death of the patient, there may be either a fatal rupture of the heart through the weakened necrotic area, or an organization of the infarct with its replacement by a patch of scar tissue. This may be able to withstand the intracardiac pressure or it may gradually give way with the resulting formation of a cardiac aneurism.

The *symptomatology* of acute coronary obstruction has been greatly clarified during the past decade and in this work American clinicians have been prominent. The condition occurs most commonly in males during the fourth and fifth decades of life. The patients may be divided into three groups according to their past history: (1) those in apparent health in whom the symptoms appear out of a clear sky; (2) those with a previous history of anginal attacks and (3) those in whom the coronary obstruction is an incident in the course of an already existing heart failure.

The *onset* is sudden and usually, though not invariably, painful. It is not dependent on effort but may come on during sleep. The *pain* is variable in location, often midsternal, but not infrequently behind the lower end of the sternum or epigastric. It is intense, often squeezing or pressing, and may radiate to the back, the arms or the abdomen. Patients who have suffered from anginal attacks usually recognize it as more severe or different in quality from their previous attacks. It lasts much longer than the pain of ordinary angina pectoris and is usually uninfluenced by the nitrites. It may recur paroxysmally over periods of hours or even days constituting the so-called *status anginosus*. Usually urgent dyspnoea accompanies the pain and in those patients in whom pain is absent dyspnoea is often a prominent feature. The pain may also be accompanied by pronounced gastro-intestinal symptoms, particularly vomiting and intestinal distention. With these symptoms there is usually a feeling of intense prostration. In those patients who survive, and in the severer cases death may occur almost instantaneously or in a few hours, the pain may disappear with great relief to the patient who still, however, remains extremely prostrated.

The *physical signs* are often quite characteristic though, in the milder cases, they may be far from striking. The patients often present the appearance of shock. Their color, as Libman points out, may be a peculiar ashen gray, the forehead may be bathed in sweat, the extremities

cold and the pulse small and rapid. They do not usually assume the fixed position of patients with ordinary angina pectoris and may be restless and anxious. Some, as Herrick points out, are distinctly euphoric in their outlook. After twenty-four hours or more, fever, usually from 100° to 102° F. is commonly present and the blood shows a moderate leukocytosis.

The *circulatory findings* naturally depend upon the extent and situation of the heart muscle involved. The pulse is variable. It is usually weak and rapid and often regular. In case the conduction apparatus is involved, it may be slower than normal or may show irregularities, most commonly extrasystoles, occasionally auricular fibrillation or block. The blood-pressure varies at different stages of the process but it is very common to find a decided drop at the onset. The heart sounds are, as a rule, decidedly feeble and this is further accentuated in some cases by an accompanying acute emphysema. Heart murmurs, usually systolic in time, are likely to be present in patients with preëxisting heart failure and occasionally in others. A localized pericardial friction rub, the so-called *pericarditis epistenocardica*, may be heard in a certain proportion of the patients and is of great value when present. The bases of the lungs usually show numerous fine moist rales and in some instances these are widely distributed throughout both organs. Considerable enlargement of the liver from acute congestion is quite common. Abdominal distention, at times accompanied by considerable rigidity and even by marked upper abdominal tenderness is not unusual.

In many cases the electrocardiograph is of great value in confirming the diagnosis. While there is no absolutely characteristic picture, disturbances of the *T*-wave, lengthening of the *Q-R-S* complexes or other evidences of damage to the conduction system are of great value when considered with the clinical features.

In the patients who do not die within the first few hours the outcome depends on the extent and localization of the cardiac damage. Some patients after surviving for several days may die with great suddenness from cardiac failure. Two of my patients died of cerebral emboli and Herrick has also noted embolic phenomena. Terminal pneumonia causes some deaths. Some patients survive for months with the signs of heart failure and some recover sufficiently to be able to lead a quiet life with comfort for many years.

The *diagnosis* of acute coronary obstruction is not always easy. In some cases the picture so closely resembles the so-called "surgical abdomen" that operations for pancreatitis, ruptured gall-bladder or peptic ulcer have been undertaken. Pneumonia has at times been suspected but the absence of fever and leukocytosis at the onset and the early signs of great circulatory depression should prevent such a mistake. Acute pneumothorax or total collapse of the lung might be suspected but should be ruled out by physical examination. There is no doubt, as Herrick suggests, that many of our prominent citizens who are recorded as dying of "acute indigestion" or "ptomaine poisoning" are the victims of coronary obstruction.

Embolism and Thrombosis of the Retinal Vessels.—Embolism of the central artery of the retina is no longer believed to be so common as

was once taught. Many ophthalmologists now hold the opinion that the changes commonly ascribed to embolism are often due to arteriosclerosis or to spasm. The lesion is nearly always unilateral, affects the left eye most frequently, is more common in men than in women, and occurs most often in connection with cardiac disease. The changes occurring in the retina are essentially those which result in an anemic infarct elsewhere. The changes produced by the plugging of the central artery of the retina lead to a characteristic ophthalmoscopic picture. There is a marked ischemia of the retina with oedema. The pulsation of the arteries is absent, and these vessels appear collapsed and thread-like. The veins as well as the arteries are at first narrowed, but later may be irregularly dilated. There is commonly a blood-red spot in the fovea. The disturbance in the blood supply to the optic nerve leads to atrophy.

The most characteristic *symptom* of obstruction of the central artery of the retina is sudden loss of sight. If the obstruction is complete, the blindness is also complete. In partial obstruction there may be temporary loss of vision followed later by complete loss. If a branch of the vessel is occluded, the loss of sight affects only that portion of the retina supplied by the branch. Inasmuch as the embolism ultimately results in optic-nerve atrophy, blindness is usually permanent. In some patients, either through the establishment of a collateral circulation or as a result of a breaking up and dislodgment of the embolus, a partial return of vision occurs. Thrombosis of the central vein of the retina produces very similar symptoms, although the loss of sight is at first not so marked. In this case the ophthalmoscope shows great dilatation of the veins, contraction of the arteries, papillitis with marked hemorrhages, and ultimately optic atrophy. The diagnosis and prognosis of embolism differs according to the location and character of the obstruction, and is discussed under the various forms and situations of embolism.

Treatment.—Inasmuch as by far the commonest sources of embolism are venous thrombosis and cardiac disease, preventive measures are to a limited degree possible. The latency of certain types of venous thrombosis is to be borne in mind, and in diseases like chlorosis in which obscure pains in the legs may indicate deep thrombosis, careful examination should be made, and if any suspicion of involvement of the calf veins exists the patient should be kept completely at rest. In puerperal women also, and in patients who have had abdominal operations, the possibility of thrombosis and its frequent latency should be kept in mind, and complete rest, care in avoiding straining at stool, and the avoidance of sudden movements should be enjoined until the time of danger is past. In outspoken peripheral thrombosis avoidance of manipulation of the thrombosed vein by the physician, absolute rest, the avoidance of straining and coughing, and of too abrupt movements have already been mentioned, and are more fully discussed under the treatment of thrombosis.

Little can be done to prevent the occurrence of embolism in cases of cardiac thrombosis of the ordinary parietal type. The cardiac stimulation necessary in such patients may actually increase the danger of embolism and instances in which the administration of digitalis has been followed by evidence of the lodgment of emboli are by no means unknown. In recent years the occurrence of emboli following the adminis-

tration of quinidin for auricular fibrillation has been noted not infrequently. In acute vegetative endocarditis, measures having a sedative effect on the heart, such as the application of an ice-bag to the precordium, render the likelihood of embolism less.

The prevention and treatment of *air embolism* require separate discussion. Inasmuch as the danger is greatest during operations on the neck, the surgeon should take special pains when operating in this situation to avoid wounding the large veins. It has been proposed by Lafargue to operate under water in such cases, but this seems impracticable. It is important to keep the wound moist, for, according to Tillmanns, air embolism only takes place when the wound is dry. If air embolism has actually occurred, the surgeon, if observant, can prevent the entrance of further air by quickly placing the finger over the opening in the vessel, and if but a small amount of air has entered, this may suffice to save the patient from serious symptoms. If the patient shows marked evidences of air embolism, three methods of procedure are available: the direct aspiration of the air from the heart, forcing the air onward and getting it beyond the heart cavities and pulmonary vessels, and forcing the air in a direction opposite to the circulation out of the wound through which it entered. Direct aspiration of the right side of the heart has, so far as we know, been used only in animals. Its use in human beings is worth considering. Attempts to force the air onward may be made by introducing saline solution into the circulation through the wound in the vein, or may be brought about indirectly by attempting to make the patient cough or vomit. In some instances it has been possible to force the air out of the opening in the vein by rhythmical compression of the thorax, allowing the opening to remain open while the compression is being made and closing it at other times. As air embolism is so rapidly fatal, promptitude on the part of the surgeon is one of the chief considerations.

In the prevention and treatment of *fat embolism* little can be done. Inasmuch as the commonest cause is fracture of long bones, care should be taken in the treatment of such injuries to use as little manipulation as possible. In operations on the long bones also the surgeon should avoid unnecessary trauma, and in the application of brisement forcé, especially when large joints are involved, the danger from fat embolism should be borne in mind, and the procedure carried out as expeditiously as possible. The opening up of closed wounds and the ligation of vessels leading from the wound have been suggested in the treatment of fat embolism, but these procedures are little likely to be of value. Attempts to emulsify the fat by the introduction of sodium bicarbonate into the circulation seem farcical considering the weak solutions which can safely be used and the tremendous dilution which results. Efforts to dissolve the fat by the introduction of ether into the circulation are positively dangerous considering the fact that thrombosis may be produced experimentally by the introduction of ether in this manner. The most that can be done is to treat the patient expectantly, paying special attention to cardiac stimulation. There would seem to be some danger in too active cardiac stimulation, for the sudden forcing of large numbers of fat emboli through the pulmonary capillaries into the general circulation might produce serious cardiac and cerebral disturbance.

The treatment of *pulmonary embolism* has for its objects first, the support of the heart, which is usually very much depressed, and, secondly, the prevention of the dislodgment of other emboli. Immediately after the lodgment of a pulmonary embolus active cardiac stimulation must be employed, as at this time the cardiac weakness is often extreme and may be the cause of death. The usual diffusible cardiac stimulants must be promptly employed in adequate doses. Ammonia, ether and epinephrine may be given for their immediate effects, to be followed by digitalis, caffeine, or strophanthus. The object of this cardiac stimulation is to tide over the dangerous period of heart depression. When this has been done cardiac stimulants must be used with great caution, as overstimulation may lead to the loosening of other emboli and cause a fatal issue. It is well to rely upon the milder cardiac tonics after the first cardiac depression has been overcome.

The main indication for the prevention of other emboli is absolute physical and mental rest. For this purpose morphine is generally needed at first, but after a few days the marked restlessness which often accompanies the lodgment of a pulmonary embolus usually disappears, and the milder sedatives, such as the bromides, are sufficient. The prevention of coughing by pulmonary sedatives and the prevention of straining at stool by keeping the bowels loose cannot be too strongly insisted upon. The rest for the first eight or ten days should be as nearly absolute as possible. After this limited movements are allowable, but the patient should remain in bed from four to six weeks, and avoid any violent exercise for months after convalescence is established. The diet should at first be liquid, as this allows the patient to be fed with a minimum of exertion on his part. After a week or ten days a soft diet may be allowed and this may be gradually modified until the patient is on ordinary diet. Tea, coffee, and alcohol are best avoided. Pain from pleurisy and complications, as empyema and pneumothorax, are to be treated in the usual way.

The treatment of *embolism of the arteries of the extremities* has for its object the relief of immediate symptoms like pain, and the encouragement of the formation of collateral circulation. For the pain, which is frequently very severe, morphine is generally needed, and in embolism it is often necessary to continue its use for some time, for, unlike thrombosis, in which condition the pain rapidly recedes, embolism is often accompanied by an increase in suffering with the advent of gangrene. Local applications over the vessels in the form of unguentum hydrargyri, or 30 per cent. ichthyol in glycerin or lanolin, and applications of moist heat have been recommended. In applying any local medication, direct pressure on the vessel should be avoided. Little can be done to encourage the formation of a collateral circulation unless the necessary anastomoses are present. The limb should be placed in a position which favors the flow of blood to it, moist heat should be applied to the surface, and judicious cardiac stimulation should be employed. When gangrene occurs surgical treatment is necessary. The occurrence of venous hyperemia is to be avoided. Strict asepsis should be carried out to prevent infection of the necrotic part, and finally amputation is indicated. This should

not be performed until a well-marked line of demarcation has formed and the inflammation in the neighboring tissue has subsided.

The treatment of *embolism of the central artery of the retina* is unsatisfactory. It is claimed that good results have in some instances followed massage of the eyeball, the object of this being to break up the large embolus and force it from the trunk of the retinal artery into the smaller branches, where it could do less damage. The occurrence of an embolism of the retinal artery should call attention to the danger of a similar lesion elsewhere, and demands a careful examination of the patient with the injunction, if it seems necessary, of complete rest for some time.

PHLEBITIS

Inflammation of the veins is the most common form of vascular inflammation. The process may be acute, subacute, or chronic; may originate in the tissues about a vein as a periphlebitis, may begin as a lesion of the intima, an endophlebitis, or rarely, may start in the middle or external coats of the vessel.

Etiology.—Phlebitis is usually a secondary rather than a primary disease, and commonly results from trauma, from the direct extension of inflammation from a local inflammatory process, or from the metastasis of infectious or toxic material from foci of inflammation elsewhere in the body. Instances of so-called “idiopathic” phlebitis are not lacking, but the term “idiopathic” indicates little but a lack of exact knowledge.

The etiology of phlebitis from trauma needs no special comment. Phlebitis resulting from direct extension is common, and occurs in connection with most local inflammations. Certain forms of phlebitis from extension are especially prominent on account of their frequency and their danger. Among these may be mentioned septic phlebitis of the uterine and peri-uterine veins accompanying puerperal infection, phlebitis of the prostatic veins in gonorrhœa, phlebitis of the veins of the intestine in appendicitis, dysentery, and hemorrhoids, phlebitis of the cerebral sinuses in mastoiditis, and phlebitis of the umbilical vein in the newborn. In local inflammations of the peripheral soft parts, of bones, and of other viscera than those mentioned, phlebitis also occurs, but is of less moment because less apt to give rise to severe secondary manifestations. The exciting cause of the phlebitis is naturally the same organism or organisms which caused the original inflammation. In puerperal sepsis the streptococcus is most common, in gonorrhœa the gonococcus; in appendicitis and mastoid disease the pyogenic cocci, often associated in the former instance with the colon bacillus.

Multiple phlebitis of a metastatic character may accompany general sepsis, but the disease is most frequently seen in single vessels as a complication or a sequel of the various acute infectious or toxic diseases or of certain cachectic states. Inasmuch as in most instances this form of phlebitis is accompanied by thrombosis of the affected vessel and the symptoms of thrombosis usually dominate the clinical picture, the discussion of the etiology of thrombosis contains most of the information bearing on the cause of thrombophlebitis.

In the instances of phlebitis following anemic and cachectic conditions

and associated with gout, doubt as to the exciting cause prevails. In anemia and cachexia the increased predisposition to infection produced by the primary disease is well recognized, but while there is some evidence that infection plays a part in producing the secondary phlebitis, it is not yet conclusive. In the case of gout there is, besides the general predisposition to infection, the peculiar vulnerability of the cardiovascular system which is so common in this disease. Here again it is not clear whether the phlebitis is due to the same poison which causes the joint lesions or to a secondary action of bacteria or their toxins.

Chronic phlebitis is usually associated with chronic inflammatory lesions in the neighborhood of the affected vein or with a condition of passive congestion. It may also be caused by the entrance of animal parasites or their ova into the vessels, the commonest and most characteristic example of this being the chronic endophlebitis caused by the bilharzia worm (*Schistosomum hematobium*).

In all forms of phlebitis personal predisposition must not be forgotten. There is just as much reason to believe that certain individuals have particularly vulnerable veins as that other individuals have especially vulnerable pulmonary tissue. Instances of a family tendency to vascular disease, and especially to certain forms of phlebitis, are not rare.

Pathology.—The pathological picture presented by a vein which is the seat of phlebitis varies with the duration and character of the lesion. In acute phlebitis resulting from the extension of surrounding inflammation the vessel wall is usually somewhat thickened, perhaps translucent-looking and red or grayish-red in color. Actual purulent infiltration of the vessel wall may be appreciable to the naked eye. On opening the vessel the lumen is found to be filled with a thrombus of the white or mixed variety which may be in a condition of purulent softening, or, if the process has lasted some time, may show signs of organization. The microscope shows in such a vein an infiltration of the vessel wall with polynuclear leukocytes, a spreading apart of groups of cells by the inflammatory exudate, an extensive destruction of the finer fibres of elastic tissue, and sometimes actual necrosis of patches of the vessel wall. In ordinary thrombophlebitis the process is similar, but the evidences of inflammation are less marked. The changes which occur when recovery takes place have been described in the article on Thrombosis. Regeneration of the tissues follows the organization or absorption of the thrombus and is participated in not only by muscle and connective tissue, but also by the elastica. In some instances acute phlebitis is not accompanied by thrombosis, and this is especially apt to be the case in certain types of phlebitis of the superficial veins.

In chronic phlebitis there is a thickening and stiffening of the vessel wall which may or may not be accompanied by thrombosis. This is often associated with distinct dilatation of the vessel. Microscopic examination of such a vein shows an increase in the cells of the intima which may be either diffuse or patchy, an hypertrophy of the musculature, and an increase in the connective tissue throughout all coats, but especially marked in the adventitia. There may be a marked increase in the elastic fibres of the vessel wall and the vasa vasorum may be considerably dilated and show proliferative changes in their lining endothelium.

In infection with the *bilharzia* the phlebitis which results is a pure endophlebitis. The intimal cells proliferate and produce bud-like projections which invade, and sometimes completely fill the lumen of the affected vessels. There is also proliferation of the subendothelial coat of connective tissue. This form of phlebitis is, however, never accompanied by thrombosis.

Besides these varieties there is a special type of phlebitis which has been described by Neisser¹ and by Schwartz² as *phlebitis migrans*. In this type the lesion appears to the naked eye as a fusiform swelling of the wall of the vein, sharply localized, not seriously impairing the lumen of the vessel, and not accompanied by thrombosis. Under the microscope this swelling is found to be due to the infiltration of a localized area of the outer and middle coats of the vessel, with a richly vascularized granulation tissue. In Neisser's specimens, taken from patients who had a luetic history, the collections of cells were more or less closely grouped about the small vessels, and were interspersed between areas of relatively normal tissue. In Schwartz's specimens, from patients with tuberculosis and phlebitis migrans, the cell infiltration was much more diffuse.

The occurrence of specific tuberculous and syphilitic phlebitis needs only brief mention. Tuberculous phlebitis is of little direct clinical import, though its relation to acute miliary tuberculosis of the lungs renders it of great pathological significance. Syphilitic phlebitis occurs as gumma formation in the walls of the veins. It also is of pathological rather than clinical significance. There are instances of obliterative phlebitis in connection with intestinal and pancreatic syphilis which are probably syphilitic, but which present no pathognomonic histological changes. The specific nature of doubtful venous lesions may be cleared by finding in them the *Treponema pallidum*. An extensive discussion of syphilitic phlebitis may be found in the monograph of Proksch.³

The favorite sites of phlebitis differ according to the cause. Traumatic phlebitis, the form following the infectious and cachectic diseases, and so-called gouty and rheumatic phlebitis usually attack the veins of the extremities, the lower extremities much more frequently than the upper, and the left side much more frequently than the right. The veins of the lower extremities are probably most frequently attacked on account of the greater chances of obstruction to the return flow of blood in them, especially in patients with feeble circulation, the greater strain to which the vessels are subjected from the action of gravity, and their greater liability to trauma. Phlebosclerosis, which is held by some authorities to predispose to attacks of acute phlebitis, is also more common in the veins of the lower extremities. The reason why the lesion occurs more frequently on the left side is not clear. Phlebitis from extension naturally occurs most frequently in those situations where acute inflammation is common, as the skin, the alimentary tract, and the lungs.

Symptoms.—Acute phlebitis may cause both general and local symptoms. The general symptoms may precede the local ones. The patient may feel unwell, and there may be a slight fever and a gradually increasing pulse rate before any appreciable local evidences of phlebitis appear.

¹ *Deutsch. med. Wchnschr.*, 1903, **29**, Nr. 37.

² *Virchow's Archiv*, 1905, **182**, Heft 2.

³ *Ueber Venensyphilis*, Bonn, 1898, Handstein.

When the phlebitis is septic in origin the fever may be intense and the illness may begin with a chill. Ordinary cases of phlebitis do not, as a rule, have fever higher than 101.5° to 102° F., and this usually subsides a few days after the onset. Very often the occurrence of pain, most marked at the site of inflammation, but usually radiating more or less, is the first symptom. The symptoms and signs which develop after the first few hours depend upon the presence or absence of thrombosis. In most instances the vessel becomes plugged by a thrombus and the symptoms described in the article on Thrombosis occur. Thrombosis does not always occur, however, and is more commonly absent in phlebitis of superficial veins than in phlebitis of deep veins. In case it is not present the inflamed portion of the vein is apparent as a semi-elastic, tender cord, the skin over which is often reddened. There is usually some local inflammatory oedema of the tissues over the vessel. The absence of thrombosis may be tested by compressing the vein at a point between the inflamed area and the heart, and determining whether the blood is dammed back by this procedure. Phlebitis of the veins of the limb is usually accompanied by a certain amount of stiffness and disability, especially if the inflamed vein be in the neighborhood of a joint. This stiffness is due to the pain which is produced by movement of the affected limb, and is not a paresis or paralysis. When thrombosis does not occur, the acute signs of phlebitis usually begin to disappear in two or three days, and in ten days or two weeks the vein may have returned to normal.

The clinical picture presented by the so-called "phlebitis migrans" is a little different from that of the ordinary acute phlebitis. Phlebitis migrans may occur during the tertiary stages of syphilis or in patients who have no specific history. It attacks by preference the veins of the upper extremities, especially those about the bend of the elbow, and appears in the form of multiple spindle-shaped swellings averaging 3 or 4 cm. in length by 1 cm. in diameter. These swellings appear along the course of a single vessel or may be distributed on several vessels. They are usually somewhat sensitive to the touch, are firm but elastic, and may or may not be accompanied by evidences of inflammation of the overlying tissue. Sometimes the skin over them is pale and free from all signs of inflammatory change; in other instances it is distinctly reddened. A slight but distinct inflammatory oedema, usually pretty well confined to the region of the inflamed patch, is sometimes present. This form of phlebitis is never associated with thrombosis. The veins distal from the the enlargement show no engorgement and there is no general oedema of the area supplied by the inflamed vessel. In a few instances sensory changes in the fingers, in the form of slight paresthesia, have been described. The peculiarity of this form of phlebitis which gives it its name is the fact that the fusiform swellings on the vessels may actually progress from one part of the vessel to another. Measurements taken from day to day have shown that the swelling may occasionally change place to a slight extent. So far phlebitis migrans has only been observed in connection with syphilis and pulmonary tuberculosis, but it will probably be shown that it is not invariably associated with these diseases.

Acute suppurative phlebitis is always accompanied by thrombosis, and besides causing the ordinary signs of thrombo-phlebitis, it is commonly

associated with indications of a general sepsis. There may be fever of an intermittent type, chills, profuse sweats, rapid action of the heart, and the presence of a marked leukocytosis. This form of phlebitis is most common in the deeper peripheral veins, in the hemorrhoidal veins, the uterine veins, the cerebral sinuses, and the portal vein and its branches. The symptoms of the varieties of suppurative phlebitis of medical interest are considered in the article on Thrombosis.

Chronic phlebitis gives rise to the same symptoms as the acute variety, although their intensity is less. It is very apt to be marked by a series of exacerbations, during which the pain and symptoms of inflammation become more marked, alternating with a series of remissions. It may or may not be accompanied by thrombosis, and, just as in the acute form, the symptoms will depend to a considerable extent on this factor.

Sequelæ.—These depend in the main on the presence or absence of an accompanying thrombosis. If thrombosis is absent, a complete return to normal of the vessel is frequently observed. If thrombosis is present, the element of importance is the character of the thrombus. If a bland one, it may be absorbed and the vein return to normal, or it may become organized and the local sequelæ of thrombosis may be left behind. If the thrombus is septic or associated with certain diseases, as chlorosis or puerperal infection, there is considerable danger of embolism, and this is the most serious complication of phlebitis.

In certain forms of phlebitis there is a strong tendency to recurrence. This is true of syphilitic phlebitis, of idiopathic recurrent thrombophlebitis, and of thrombo-angitis obliterans. In syphilitic phlebitis the tendency is for the recurrence to attack different veins each time. In idiopathic recurrent thrombophlebitis the process attacks successive segments of the same vessel, usually until it has completely obliterated it.

Diagnosis.—The diagnosis of phlebitis of a superficial vein is usually a simple matter. The sudden onset with pain, the slight constitutional symptoms, and the thickened vessel with the overlying, reddened, œdematous skin leave little room for error. In some instances of thrombophlebitis there are sources of error, as described in the article on Thrombosis. Here also is to be found the discussion of thrombophlebitis of the veins of the different viscera and of the different vessels.

Prognosis.—This hangs upon the concurrence of thrombosis, and depends almost entirely upon the character and location of the thrombus. For this reason it is discussed under the head of disease associations and special form of thrombosis in the article on Thrombosis. Simple phlebitis unaccompanied by thrombosis has almost invariably a favorable outcome. The tendency of some forms to recurrence should be borne in mind in giving a prognosis.

Treatment.—This is essentially that of thrombosis; it depends on the cause and situation of the lesion, but is mainly influenced by the fact that thrombosis is usually present. In a few forms, such as syphilitic phlebitis, specific internal treatment is demanded; but, as a rule, the treatment consists of relieving the pain by general and local treatment, and putting the patient completely at rest. The excision of the inflamed area of vein, as recommended by the French school and by Moullin, may be advisable in some cases.

CHAPTER XXV

THE DISEASES OF THE LYMPHATIC VESSELS

BY ALDRED SCOTT WARTHIN, PH.D., M.D.

Introduction.—The diseases of the lymphatic vessels have hitherto been accorded but slight attention in works on internal medicine. In fact, in the majority of these no separate treatment of this subject is deemed necessary, and only passing allusions are made to pathological conditions of the thoracic duct or peripheral lymphatics in their connection with more general pictures of disease. This is due in part to the fact that the lymphatic system, having its roots in the minute lymph canaliculi of the various organs and tissues, stands in such intimate relationship to the parenchyma that pathological changes in one usually mean the involvement of the other, so that it becomes possible only in rare cases to separate the pathological anatomy of the smaller lymphatics from that of the organ or tissue concerned. The diseases of the lymphatics likewise are so closely related to those of the veins that a clinical separation is usually not attempted. Even in the case of the larger lymphatic channels it is rarely possible to distinguish independent pathological conditions. Inflammation, tuberculosis, or malignant disease of the thoracic duct may be wholly masked by the septicemia or pyemia, general miliary tuberculosis, or metastases dependent upon these conditions. To such an extent is this true that some writers have denied to affections of the lymphatic vessels any independent symptomatology aside from that resulting from obstruction to the outflow of lymph, such as œdema, chyluria, chylous ascites, chylothorax, chylopericardium, etc. As it is, many of these cases are relegated to surgery for final consideration, and for this reason the pathology of the lymphatics has been more adequately treated in surgical works than in those of internal medicine. With careful analysis the diseases of the lymphatics must come to hold a more independent and important position. This is true particularly of the thoracic duct and its branches. Only those forms of disease of the lymphatic vessels that possess a definite clinical significance are considered here.

1. DISEASES OF THE THORACIC DUCT

General Considerations.—The thoracic duct is the main trunk of the lymphatic vascular system, and receives the chief portion of the lymph from the peripheral lymphatics. It is formed by the union of the lumbar lymphatic trunks (*trunci lumbales*), that convey the lymph from the lower extremities, pelvis, genitalia, and abdominal wall, with the intestinal trunk (*truncus intestinalis*), into which the chyle vessels empty. At the

point of union, which varies greatly (*low position* at the level of the first or second lumbar vertebra; *high position* at level of eleventh or twelfth thoracic vertebra), a dilatation is usually found (*receptaculum* or *cisterna chyli*). This sac, however, is not always present, and its place may be taken by a plexus of lymphatic vessels. Passing through the aortic opening in the diaphragm, the duct ascends in the posterior mediastinum to the right of the median line, lying between the aorta and right vena azygos. At the level of the fourth dorsal vertebra it turns to the left and ascends on the M. longus colli to about the height of the sixth cervical, and, after receiving the lymph trunks from the upper portion of the body, empties into the left subclavian vein just before its union with the left internal jugular.

The routine examination of the thoracic duct in autopsy work has been much neglected, owing to the prevalent mistaken idea that its demonstration is a matter of great difficulty. As a matter of fact, it is easily found. If, after the removal of the heart and left lung, the right lung is turned over into the left side of the thorax, and the tissues on the right side of the posterior mediastinum and the overlying pleura are put on the stretch, it is but rarely that some portion of the duct is not recognized through the delicate pleural covering or as soon as the latter has been slit longitudinally and dissected away. The greater portion of the duct can be dissected out at this time, or a thread may be tied around it to make its recognition more easy after the removal of the neck organs and thoracic vessels.

The right lymphatic duct, sometimes called the right thoracic duct, receives the lymph from the right side of the head, neck, thorax, right lung, right heart, right upper extremity, and upper surface of the liver. It is less than an inch long and empties into the right subclavian or internal jugular near their junction. Like the thoracic duct its opening has a double valve. Nothing is known of its pathology.

Anomalies.—Numerous anomalies have been described. Instead of a single duct there may be a plexus of small lymphatics extending along the entire course of the normal vessel, or the duct may be represented by two or more distinct trunks, which may run an individual course or may re-unite to form a single channel, persisting throughout the remaining portion of the course or again dividing. In the case of a double duct, one vessel may empty into the right subclavian vein, the other one into the left, or the termination may consist of a delta-like lymph plexus. Anomalies of termination are very frequent. The duct may empty into the right subclavian vein, right internal jugular, by two trunks into the right and left subclavians or the right and left internal jugulars, the junction of subclavian and internal jugular on one or both sides, the brachiocephalic vein, inferior vena cava, azygos major, etc. In the case of termination by plexus, the various trunks may empty into several different veins. Some of these anomalies of termination occur so often that they have been regarded as representing normal variations. It is because of the rapid collateral adjustment in these anomalous branches that any obstruction of the main thoracic duct so rarely leads to any lymph stasis.

The clinical significance of these anomalies is chiefly surgical. The anomalous branches may be injured by surgical procedures, particularly when the duct or ducts rise high in the neck. This occurs not infrequently in the case of a right-sided duct or a double duct. Lymph fistula or chylothorax constitutes the usual symptom. In other cases the anomalous duct or branch may be ruptured by trauma and the resulting chylothorax be regarded as a medical condition until its nature is discovered.

Absence of the thoracic duct is mentioned repeatedly in obstetrical literature as a cause of *œdema neonatorum*, but authentic observations of such an anomaly are apparently wanting.

Hemorrhage.—Hemorrhage into the thoracic duct may occur as the result of trauma to the mesentery or intestines, retroperitoneal or mesenteric hemorrhages due to congenital or acquired hemophilia (severe anemia, chronic icterus), extreme passive congestion of the portal system in hepatic cirrhosis, ruptured sac in ectopic gestation, and following pelvic operations. The entrance into the general circulation through the thoracic duct of a large amount of altered blood would offer conditions favoring thrombosis and embolism in the smaller vessels of the body. No symptoms referable to a thoracic duct condition would exist unless thrombosis occurred within the duct itself or at its mouth, obstructing it so that chylothorax or chylous ascites would occur in the absence of an adequate collateral circulation. Such cases have not yet been recognized.

Thrombosis.—Thrombosis of the thoracic duct has been observed in a number of cases. Two varieties may be described. In one the thrombus begins within the subclavian vein, at or near the mouth of the duct, and finally obstructs the latter; in the other form the thrombus occurs primarily within the lumen of the duct. The cases described by Oppolzer, Cayley, Turney, and others belong probably to the first type. Oppolzer's case was one of cardiac valvular lesion. At autopsy a thrombus obstructing the mouth of the thoracic duct was found. There was neither chylothorax nor chylous ascites present. Cayley's case presented a thrombus closing the mouth of the duct and causing such marked dilatation of the duct and the receptaculum chyli with its radicles, that the latter could be felt as a large tumor during life. In Turney's case both chylothorax and chylous ascites were present, the duct and all its radicles being dilated, while its mouth was blocked with a thrombus.

Etiology.—The causes of thoracic duct thrombosis have been given by various authors as hemorrhage into the duct, inflammation of its wall, trauma, tuberculosis, metastasis of malignant tumors, infection, presence of filariæ, pressure of neighboring tumors, aneurisms, anomalous vessels and exostoses of the vertebræ, the obliteration of the left subclavian vein, etc. Those occurring primarily in the vein at the mouth of the duct may be dependent upon a valvular lesion, or they may be infective. Carcinomatous thrombi may also have their seat at the mouth of the duct. There can be but little doubt that some of the so-called thrombi found within the thoracic duct were tubercles or tumor-masses.

Symptoms.—The symptomatology is purely one of obstruction in so far as its distinctive features are concerned. Chylous ascites alone or

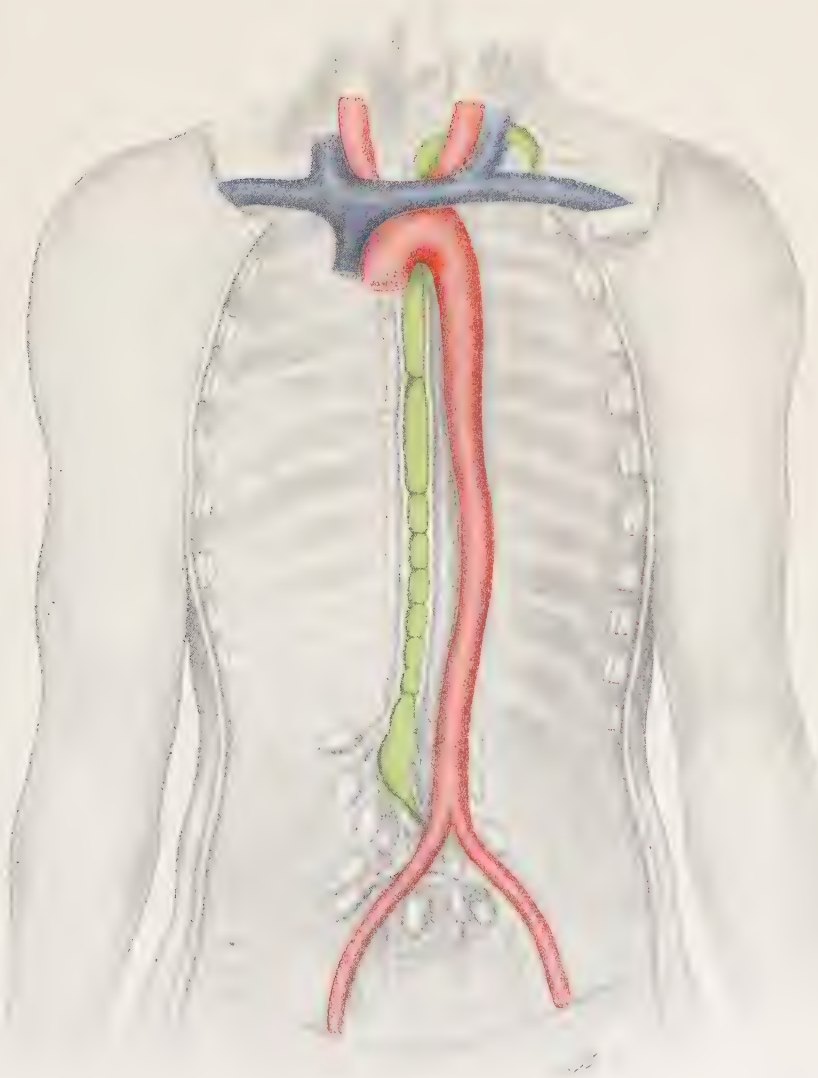
combined with chylothorax or chyluria would point to such an obstruction. The dilated receptaculum might be palpable through the abdominal wall as an elastic retroperitoneal tumor. Aspiration of such a tumor should be practised, as it might lead to a definite diagnosis of obstruction of the duct from the character of the fluid obtained. Obscure abdominal pains, intestinal disturbances, œdema or elephantiasis of the external genitals or lower extremities may occur as features of the clinical picture.

The occurrence of symptoms of obstruction, as well as their severity, will depend upon the adequacy of the collateral circulation. A thrombus located at the mouth of the duct is more likely to cause obstruction to the lymph outflow than one located nearer to the receptaculum; but, even in the former case, an anomalous termination may be able to compensate fully, and symptoms of obstruction may be wholly wanting. A thrombus slowly formed, or one that only partly blocks the lumen, is not likely to cause any symptoms of obstruction.

The thrombus may undergo simple softening, and finally disappear entirely, or organization of the thrombus and the permanent obstruction of the lumen of the duct by a mass of newly formed connective tissue canalized by new blood and lymph vessels may take place. Aschoff reports a case in which the thrombosed portion of the duct was converted into a thin tough cord. Calcification of the thrombus may take place, leading to the formation of a thoracic duct stone. The "*chyle stone*" occurring in the receptaculum, described by Scherb in 1729, is an interesting finding, and probably represents an old calcified thrombus. In cases of tuberculosis with entrance of tubercle bacilli into the thoracic duct miliary tubercles may develop in an organizing thrombus of the duct.

Fat Embolism.—In 1910 Wilms recommended the establishment of a thoracic duct fistula in the treatment of fatty embolism, on the ground that more fat is added to that in the blood by absorption through the lymphatics, the fat passing the lymph nodes and reaching the thoracic duct, whence it passes into the venous circulation some time after the fat that gained immediate entrance into the veins. This accession of fat may be the final straw in bringing about the fatal termination, and if this increase in the fat in the blood stream can be prevented the patient may survive. Wilms carried out this operation on one case of fatty embolism in a patient who fell from a window and sixteen to twenty hours after the operation became soporific, his temperature rising to 104° F., respirations to 40. Believing the entrance of the fat to be chiefly through the lymphatics, Wilms opened and drained the thoracic duct, large fat-droplets appearing in the lymph. The fistula closed on the ninth day, the patient recovering gradually. Wilms' method was used experimentally by Fritzsche (1910), who found that drainage of the thoracic duct warded off a fatal termination when the operation was performed at the first signs of danger. The risk of the operation is slight, and the consequences negligible. On the other hand, as so few patients with fatty embolism diagnosed *intra vitam* survive, the risk of the operation is nothing compared to that of the condition itself. As Grondahl says, this method of treatment is certainly theoretically a good one, and surgeons should be urged to carry it out whenever there are indications of cerebral fatty embolism.

PLATE VII



Acute Primary Suppurative Inflammation of the
Thoracic Duct. (De Forest.)

(*Bacillus pyocyaneus*.)

Inflammation.—A number of cases have been described; in the majority it has been purely secondary to inflammatory processes involving the chyle vessels and the pelvic radicles. In dysentery, suppuration of the mesenteric glands, pelvic suppurative processes, etc., the entrance of bacteria into the mesenteric and pelvic lymphatics is probably the rule, but in the majority of cases they appear to pass on with the lymph into the blood stream without causing local lesions in the duct or its radicles. In rare cases an ascending thrombo-lymphangitis of the duct occurs. It is not improbable that the thoracic duct becomes the most important portal of entrance into the blood stream of pyogenic organisms coming from local lesions in the territory drained by it. It plays, therefore, a very important rôle in the causation of pyemia and septicemia. The metastatic abscesses occurring in dysentery may well owe their origin to a transportation through the thoracic duct. Likewise, the entrance of gonococci into the blood stream may occur chiefly through the thoracic duct, as it is now known that the gonococci gain entrance to the lymphatics of the genitals and pelvis. In some cases the walls of the duct may become the seat of a purulent inflammation, and at autopsy the lumen may be found to contain pus. The independent nature of the thoracic duct suppuration is not clear in these cases.

In a case of purulent salpingitis in a young girl convalescing from smallpox seen by the writer, the pelvic and mesenteric lymphatics were the seat of a marked suppurative inflammation, the receptaculum and the thoracic duct being similarly involved. All the organs contained pyemic abscesses. Aside from the high leukocytosis (70,000), there were no symptoms that could be connected with the thoracic duct involvement.

Few observations exist of independent inflammation of the duct. Enzmann gives 6 cases as representing this condition, but the evidence is unsatisfactory. De Forest¹ has reported at length a case of *purulent inflammation of the duct*, apparently primary in character. The patient, who had shortly before had an attack of "ptomaine poisoning," became ill after partaking heartily of "cold-storage poultry," and developed nausea, followed by chills and fever, passing finally into a condition resembling typhoid fever, death taking place on the twenty-fourth day. At autopsy no evidences of typhoid fever were found, but the thoracic duct was distended to the size of a bologna sausage and filled with foul pus of a bluish-color. (See Plate VII.) The constrictions at the valves gave it a peculiar sacculated appearance. Pressure upon the duct caused pus to trickle slowly through the terminal valve into the vein. The mesenteric glands, particularly those near the duct, were enlarged. No primary purulent process was found in the intestine or elsewhere, and there were no metastatic abscesses. Cultures were not made, but from the character of the pus the *B. pyocyaneus* was supposed to be present.

The clinical symptoms of this interesting case were those of a septicemia, passing into a typhoidal state. The positive evidences of typhoid fever were lacking; and two symptoms were present that in the light

¹ *New York State Journal of Medicine*, September, 1907.

of the autopsy findings might be regarded as pathognomonic. The extremely high leukocytosis, the white cells before death reaching nearly 200,000, and the rather unusual production of nausea whenever the patient was turned upon his side were the only clinical features that can be taken to form a basis for a differential diagnosis. The sausage-like tumor might possibly have been felt by deep palpation. Otherwise the clinical picture appears to be that of a septicemia of unknown origin.

It is probable that the condition described in 1831 by Nothher as a "gangrenous thoracic duct," which was found at autopsy a few hours after death in a patient dying of a "malignant epidemic fever," may have been similar to De Forest's case. Other cases of the same nature may exist and go unrecognized, either through the failure to perform an autopsy or because of an incomplete examination. The clinical diagnosis of such a condition has never been made up to the present time. In the case of a septicemia or toxemia of unknown origin, a progressively increasing leukocytosis up to very high counts might direct suspicion toward the thoracic duct as the seat of a purulent inflammation. The symptom of nausea mentioned above may be found to have some worth. Deep palpation with the patient in a warm bath should be tried. In the case of a localized abscess, involving some portion of the duct, the symptom of chylothorax or chylous ascites may be added. Finally, an exploratory operation might settle the matter and serve as a therapeutic measure in those cases in which the receptaculum or the abdominal portion is involved.

Chronic inflammation of the thoracic duct has been described in the literature. Andral mentions a constriction of the lumen of the duct by a formation of scar-tissue in its wall at the level of the fifth dorsal vertebra. Heller found in a woman, fifty-six years old, who had suffered from ascites and marked œdema of the pelvic tissues, that the wall of the duct was greatly thickened and its lumen almost obliterated. He regarded the condition as the result of a chronic inflammation of the wall of the duct. Other similar cases of supposed chronic lymphangioitis of the duct have been reported, but it is clear from the descriptions that the condition was one of tuberculosis or infiltration of the wall of the duct by a malignant neoplasm. Thus the case reported by Schweninger, of *lymphangioitis proliferans* of the duct was undoubtedly one of carcinomatous infiltration. Likewise, the classical cases of Cheston and Assalini, in which the duct was filled with bony masses, have been passed along in the literature under the terms "calcification," "ossification," and "*lymphangioitis ossificans*" of the duct. Certainly, the description given by Cheston leaves no doubt that the duct had been invaded by an osteosarcoma primary in the pelvis. Inflammation of the thoracic duct due to syphilis, parasites (*filaria*), etc., is hinted at in the literature, but without actual pathological demonstration.

Tuberculosis.—The thoracic duct is one of the most important channels by which great numbers of tubercle bacilli are rapidly disseminated throughout the body, and it, therefore, is one of the chief avenues concerned in the production of acute general miliary tuberculosis. It has been definitely shown that tubercle bacilli may pass the intestinal wall

without the production of local lesions, enter the lymph stream and pass through the thoracic duct into the blood and produce lesions first in the lungs. The duct itself may be the seat of tuberculous lesions, from which the bacilli are carried in great numbers by the lymph into the general circulation; or the duct, while in itself not affected, may be the avenue through which great numbers of tubercle bacilli, given off from a tuberculous lymph node, may pass with the lymph into the blood stream. Further, a subacute or even chronic tuberculosis may result when a small, caseous tubercle occurs in the duct, giving off from time to time into the lymph stream, a small number of bacilli. The more carefully this condition is studied at autopsy the higher the percentage of thoracic duct lesions discovered. In a series reported by Longcope the duct was affected or contained tubercle bacilli in over 79 per cent. of cases of acute miliary tuberculosis. Whipple reported a series of cases in which smears from the contents of the duct showed tubercle bacilli in all cases in which the mesenteric glands were involved. Tuberculosis of the thoracic duct cannot be regarded as rare, and its relation to general miliary tuberculosis is more important than tuberculosis of veins and arteries.

The infection of the duct takes place usually from caseous mesenteric, retroperitoneal, or mediastinal lymph glands, although it is possible that in some cases tubercle bacilli pass through the intestinal wall without causing lesions and into the lymphatics to excite first within the thoracic duct the characteristic lesions of the disease. Ordinarily, however, the thoracic duct lesion is secondary to an older tubercle of a lymph node. In cases of endothoracic tuberculosis a retrograde metastasis into the paraortic lymph nodes of the abdomen is frequently seen.

The character of the lesion within the duct may vary greatly. There may be scattered miliary or submiliary nodules, multiple or single in the intima of the duct, or the entire wall may be studded with larger conglomerated polypoid tubercles. Caseous ulcers may be present, particularly upon the valves. In many cases there is a single large caseous nodule near the upper end of the duct, but sometimes in or near the receptaculum. The latter is sometimes replaced by a conglomerate mass containing numerous pea-sized cavities filled with caseous material. As a result of hemorrhage, these cavities may show red spots. In advanced cases the wall of the duct throughout its entire length may be thickened and caseous, the lumen in part obliterated or in part varicose, and in the latter case filled with a caseous or whey-like substance. Tubercles forming behind a valve flap push the flap out into the lumen, and so obstruct the latter. Chylous ascites and chylothorax may result from tuberculous obstruction of the duct, but this is rare, an adequate collateral lymph circulation usually being developed. Except for such symptoms of lymphatic obstruction, tuberculosis of the duct gives rise to no definite clinical picture ascribable to the affection of the duct itself, but in advanced cases the number of tubercle bacilli entering the blood stream from the duct may be very large, and a generalized miliary tuberculosis develops.

Syphilis.—Gummatous lesions of the thoracic duct or lesions of other nature definitely ascribable to syphilis have apparently not yet been observed. In congenital syphilis great numbers of spirochetes may be present in the wall of the thoracic duct without the occurrence of recognizable histological changes.

Ectasia.—Dilatations of the thoracic duct are not uncommon. They have been reported in the literature under various heads—aneurism, varicosity, cysts, etc. The duct may be dilated as a whole or in part. The nature of some of these localized dilatations is not at all clear. In part they appear to be the result of obstruction, either from within (thrombus, tubercle, carcinoma) or from external pressure upon the duct (tumor, aneurism, etc.). When the obstruction occurs at the upper end the entire duct may be dilated, presenting sausage-like sacculations, while the receptaculum is as large as a hen's egg, or even larger. In other cases no obstruction is present, and there is no evidence of pressure from within or without. On the other hand, in many cases where there is actual obstruction of the duct, no dilatation of the duct occurs. By some writers the cause of the partial dilatations or varicosities occurring without obstruction is sought in a local weakening of the wall of the duct, due to defective development or to atrophy.

There is no symptomology, or, in the event of rupture or obstruction, an associated chylothorax, or chylous ascites or chyluria, calls attention to the thoracic duct. The cystic enlargement of the receptaculum may be seen or palpated as a fluctuating retroperitoneal tumor, the contents of which may be recognized on aspiration.

Chyle Cysts.—The cystic dilatations of the radicles of the thoracic duct deserve special mention. They may occur as the result of obstruction to the duct or of its branches, as the result of local inflammation, or partake more of the nature of developmental disturbances. They are classed by different writers partly as *lymph cysts* and partly as *cystic lymphangiomas* or *chyle angiomas*. They may be solitary or the peritoneum may be studded with them. They vary in size from that of a pea to a man's head, are often pedicled or clustered like a bunch of grapes, and usually possess very delicate, thin walls. Their contents are whitish, creamy, or, more rarely, caseous. In the large ones the fluid may be clear and several liters may be present. In cases of chyle stasis the entire peritoneum is sometimes dotted with small whitish or yellowish points, corresponding to small dilatations of the chyle vessels. The intestinal folds and villi may also be studded with them. When lying close together the appearance presented is that of a lymphangioma. They may be connected by varicose cords, along which may be scattered plaques of lymphorrhagia. Small, isolated chyle cysts of this type are not at all uncommon, and are probably due to some local obstruction of a chyle radicle. It is very probable also that they bear some relation to stages of digestion. The multiple lymph cysts are usually associated with a chronic peritonitis. The larger tumors are more rare and are apparently independent of inflammatory changes. They may be found even in children, and are probably to be classed with the disturbances of development. They usually lie behind the stomach or an intestinal coil,

the percussion tone over them often being tympanitic. In some cases the stomach or intestine may be pressed so closely against the abdominal wall that only a dull percussion note is obtained and the compressed stomach or intestine may be injured by aspiration or operation. The points of differential diagnosis are, the presence of a fluctuating retro-peritoneal tumor, its location and relations, the character of the fluid obtained by aspiration, etc. The symptoms are wholly those of pressure.

Obstruction.—This may be caused by thrombosis, tuberculosis, metastatic tumors, inflammation, parasites within the duct, compression of the duct by diseased lymph glands, aneurism, neoplasm, exostoses and scar tissue, inflammatory constrictions of the duct, thrombosis of the subclavian or innominate vein, high venous pressure in cases of tricuspid insufficiency, etc. The effects vary greatly in different cases; when in the lower part of the duct an adequate collateral circulation is usually established without much damage resulting. Even with an obstruction of the terminal portion of the duct many cases may present no symptoms. In all cases in which the collateral circulation is inadequate there results a chyle stasis, with dilatation of the duct and its radicles. The chyle may escape from the distended vessels by transudation or rupture, and may infiltrate the tissues or collect in the serous cavities, giving rise to a chylothorax, chylopericardium, or a chylous ascites.

Rupture.—The thoracic duct may be torn or ruptured through trauma or surgical operation, or as the result of distention following obstruction, erosion by aneurism or tumors, etc. The deep situation of the duct protects it from trauma, but laceration has followed shot and stab wounds, fracture of a rib, severe straining or coughing, severe blows upon the abdomen, crushing of the thorax or abdomen, etc. In operations upon the cervical region the duct may be wounded, particularly when the duct runs high into the neck. The removal of the lower cervical lymph glands and the complete operation for removal of carcinoma of the breast are the operations most frequently followed by evidences of injury to the thoracic duct. The injury may be noticed at the time of operation or not until the dressing of the wound. There may be a distinct gush of milky or serous fluid, or such a fluid may slowly collect in the wound or dressings. In the case of an internal rupture, the condition of thoracic duct fistula is revealed through the development of chylothorax or chylous ascites.

While a hydrops chylosus often does not occur as the result of a thoracic duct obstruction, the conditions are quite otherwise with a rupture of the main thoracic duct trunks or the receptaculum. As a result of such a lesion a true lymphorrhagia into the thorax or abdomen takes place, even when there is no obstruction to the onward flow of the lymph.

The rupture of the duct is fatal in some cases, as the result of a rapidly developing marasmus following the loss of large quantities of chyle. Some cases heal spontaneously. Others recover after packing of the wound or ligation or suturing of the duct.

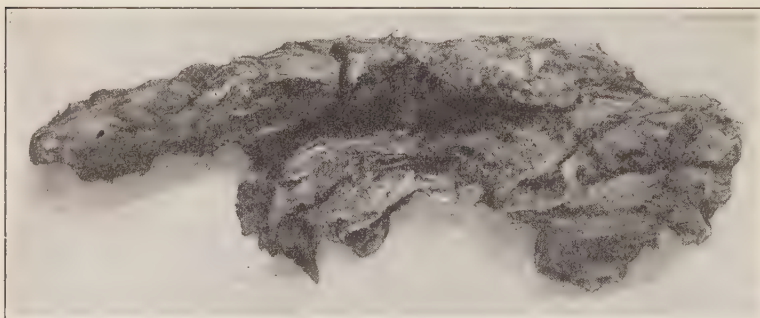
Tumors.—Primary tumors of the thoracic duct have not yet been observed. Secondary tumors, particularly carcinoma, are not infrequent, and there can be but little doubt that in the generalization of carcinomata

located primarily in the abdomen or pelvis the thoracic duct plays as important a rôle as that performed by it in the dissemination of tuberculosis. In the case of such transportation of carcinoma cells the duct may remain free itself, or may contain thrombi or tumor cells, or its walls may present carcinomatous infiltration.

Mature Connective-tissue Tumors.—No positive demonstration of the occurrence of these in the walls of the duct has yet been given. The *osteomas* and *chondromas* found metastatic in the duct were undoubtedly sarcomatous in nature. The *cystic* or *cavernous chylangiomas* or *lymphangiomas* have been mentioned above under Cysts.

Sarcoma.—But few cases of metastatic sarcoma of the thoracic duct have been reported, and there exists no authentic observation of primary sarcoma of its walls. The writer has seen several cases of metastatic sarcoma in the thoracic duct. In one case there was a sarcomatous teratoma of the testis, and in the receptaculum chyli a sarcomatous nodule completely occluding its lumen was found. Chylous ascites was

FIG. 103



Lymphosarcoma of receptaculum chyli and thoracic duct, seen from behind.
Case of chylous ascites and chylothorax.

not present. In another case (reported by Dock¹) chylous ascites and chylothorax were present in a case of *lymphocytoma* (*lymphosarcoma*) with lymphocythemetic blood, although the total number of the white cells was not greatly increased. Occupying the root of the mesentery, a large nodular lymphoid tumor was found sending up into the thoracic duct a solid cord of tumor tissue completely filling its lumen and projecting above into the left subclavian vein (Fig. 103). The walls of the duct were in part adherent to the mass and infiltrated with tumor cells. A case much resembling this one was reported by Herzog in 1899, and the writer has seen three others in children of the growth of a leukemic or leukemic lymphoblastoma through the thoracic duct. All showed chylothorax and chylous ascites.

Primary *endothelioma* of the peritoneum reaches the thorax through the thoracic duct and involves the walls of the latter.

From the few reports in the literature it would seem that secondary

¹ *Amer. Jour. Med. Sci.*, 1907, **134**, 634.

sarcoma of the thoracic duct is most likely to occur in cases of primary sarcomatous tumors of the testis, lymphocytoma of the mesentery, osteo- or chondrosarcoma of the pelvic bones, and primary endothelioma of the peritoneum.

Carcinoma.—Secondary carcinoma of the thoracic duct is not infrequent, and a fairly large number of cases has been reported since the first one seen by Astley Cooper in 1798. Schwedenberg has pointed out the great importance of the thoracic duct as the chief channel by which carcinoma cells pass from the abdominal and pelvic organs into the lungs and the systemic circulation. Actual tumor development within the duct or in its walls is not a necessary feature of such a transportation; it may occur without any involvement of the duct itself.

Of the 26 cases of secondary carcinoma of the duct collected by Winkler, the primary growth was in the stomach in 10 cases, in the uterus in 8, gall-bladder in 3, and 1 each in the testis, pharynx, ovary, adrenal, and kidney. In all of these cases secondary nodules were present in the mesenteric or retroperitoneal glands. In the 12 cases reported by Schwedenberg 4 cases were primary in the uterus, 3 in the stomach, 2 in the rectum, and 1 each in the kidney, colon, and mamma. In the last case the duct was involved through retrograde metastasis.

The appearance of the duct when it is the seat of secondary carcinoma varies greatly. To the naked eye there may be no evidence of the presence of tumor cells. Small nodules, barely palpable, may be present in the wall, or the lumen of the duct may be closed by larger masses. At other times the duct may be of the size of a finger throughout its entire length, and completely filled with tumor masses. A sacculated appearance is produced by the growth of nodules behind the valves. The lumen may be completely or partially obstructed, or the cancer mass within the lumen may be recanalized. In some cases the tumor mass is larger in the receptaculum and tapers off above. The lymph glands lying along the thoracic duct may contain secondaries when the duct itself shows no involvement, and, macroscopically, it may be difficult to say whether the latter is carcinomatous or not. The enlarged chain of lymph glands should not be mistaken for a diseased duct.

Microscopically the duct may be found to contain free carcinoma cells or masses of these. In the majority of cases thrombi are associated with the latter, and such carcinomatous thrombi are usually situated behind the valve. They are also found at the point where the duct crosses the aorta. With the growth of the tumor cells the thrombus may become organized and adherent to the vessel wall. The latter, in turn, becomes infiltrated with the tumor cells, and the inflammatory reaction dependent upon this appears as a diffuse thickening of the wall of the duct (endolymphangitis carcinomatosa). Such an inflammation and tumor infiltration may extend from the duct into the subclavian vein.

The only symptoms of secondary malignant disease of the thoracic duct that can be recognized clinically are the results of the obstruction of the duct, viz., chylothorax, chyluria, or chylous ascites. The occurrence of these conditions is dependent, however, wholly upon the inability of the collaterals to take care of the lymph stasis, and in the case of an

abundant anastomosis they may be absent. In the majority of cases a chylous hydrops does not occur. The tumor masses in the receptaculum chyli may reach such a size that they can be palpated. Enlargement of the left supraclavicular lymph nodes (less frequently the right) in connection with an abdominal or pelvic tumor is an important diagnostic sign of carcinoma metastases through the thoracic duct. Cases have been reported of advanced metastatic carcinoma of the thoracic duct without secondary growths in the lungs.

Parasites.—Cysticerci and filariæ may occur within the thoracic duct and obstruct its lumen, giving rise in some cases to chylothorax and chylous ascites, but more often to chyluria. Thrombosis of the duct may occur as the result of the presence of the parasites and the inflammatory changes set up by them in the wall of the duct.

Symptoms and Diagnosis of Thoracic Duct Disease.—A cystic fluctuating retroperitoneal tumor, containing chyle, as shown by aspiration, and located in the region of the receptaculum chyli, points to a dilatation or cyst of the duct or its radicles. Symptoms of sepsis or pyemia, with a very high leukocytosis and an elongated tumor palpable in the region of the receptaculum chyli, indicate a purulent inflammation of the duct.

Chylothorax and chylous ascites are the cardinal signs of an obstruction or rupture of the duct. Chylopericardium, chyluria, œdema of the pelvic tissues and genitalia may be associated with the other two.

Chylous Ascites.—Milky or opalescent fluids are not infrequently seen in cases of ascites. Some of these correspond so closely to chyle in their physical and chemical qualities that one has no hesitation in applying to them the term *chylous*. In other cases the lactescent fluid has been found to differ somewhat from chyle, and to such the term *chyliform* or *chyloid* has been applied. Still more rarely—in fact but one case of the kind has been reported—a milky fluid containing neither fat nor granules occurs, a *lactescent, non-chylous* effusion. Since the character of the last named could easily be ascertained by examination, the diagnostic problem of chief importance is the distinction between chylous and chyliform fluids. Some writers believe that such a differential diagnosis cannot be made from the physical and chemical characteristics, since fluid in all respects resembling chyle is found in pathological conditions of the peritoneum in which no lesion or obstruction of the thoracic duct can be ascertained. Various authors also hold that the only distinction between *chylous* and *chyliform* fluids is one of dilution or mixture, in the latter case with serous fluids of inflammatory origin. According to some, the term chylous should be used only when a definite lesion can be found in the lymphatics; in chyliform or adipose ascites, the lymphatics must present no abnormalities of any kind. The question demands some criterion by which a chylous fluid may be told from a chyliform effusion in which the milkiess is due to the presence in a serous fluid of endothelial, pus, or tumor cells undergoing or having undergone fatty degeneration. Such fluids have been found in peritoneal tuberculosis, carcinoma, sarcoma, hepatic cirrhosis, cardiac lesions, chronic peritonitis, lipemia, etc.

The character of the fluid will decide promptly in some cases. If it

is white, with numerous fat-droplets present, and forming a creamy layer on standing, and if, in addition, it contains more than 0.02 of sugar, the fluid may safely be regarded as chylous and as coming from the lymphatics. The microscopic examination of the sediment may in some cases reveal the cellular origin of the fat, but usually no trace of the cells can be seen. The absence of conditions favoring the formation of a chyloform or adipose ascites adds to the strength of a conclusion as to its chylous nature.

Cases arise, however, in which there is great difficulty in deciding whether to call an effusion chylous or chyloform. A large amount of fat and a relatively high percentage of sugar may be found in chyloform effusions when no lesions of the thoracic duct or chyle vessels can be demonstrated. It is possible that some of these fluids resembling chyle were in reality a diluted chyle, and it is highly probable that a diapedesis of chyle may take place into the peritoneal cavity through the walls of distended chyle vessels without any actual rupture.

If chylothorax is present also, the probabilities of a thoracic duct lesion are made much greater. The sudden development of anorexia, anemia, and emaciation are also regarded as symptoms favoring the existence of obstruction or a rupture of the duct. If the chylous fluid returns quickly after its removal by tapping, the probabilities are that a chyle fistula is present. In spite of these distinctions, cases of milky ascites apparently occur in which, even at autopsy, it has been impossible to say whether the effusion was chylous or chyloform.

Chylothorax.—The same difficulty exists in the case of a milky fluid in the pleural cavity, and the two forms, chylous and chyloform effusions, are likewise distinguished here. The former occurs in the event of distended or ruptured lymphatics; the latter is found in the case of the fatty degeneration of tumor, pus, or endothelial cells, in secondary carcinoma of the pleura, tuberculous and non-tuberculous pleuritis, pulmonary abscess, lipemia (?), etc. It is a relatively rare condition, and the majority of cases of lactescent pleural effusion are instances of chylothorax, and point to lesions of the thoracic duct. The same differential points hold good as for chylous ascites.

Chylopericardium.—Milky effusions into the pericardial sac are still more rare. Both chylous and chyloform fluids have been described; in one case the chylous fluid came from the rupture of a lymph vessel, in another the chyloform fluid was regarded as a transudation from a chyloform effusion in the left pleural cavity. The significance of chylopericardium in thoracic duct disease is the same as that of chylous ascites.

Chyluria.—The presence of emulsified fat and albumin in the urine gives it the appearance of chyle. Sugar is but rarely present. The appearance of chylous urine is very characteristic; it closely resembles milk, but usually contains pinkish coagula. Sometimes the entire urine coagulates on standing, or it separates into an upper creamy layer and a lower bloody stratum. Chyluria may be brought about by any obstruction to the thoracic duct, whether due to thrombosis, tumor metastases, tuberculosis, external pressure, filariae, etc. By far the most common cause of chyluria is the obstruction of the duct by either the

adult or embryonic form of *Filaria*. In northern latitudes chyluria occurring in individuals who have not been in tropical or subtropical countries is due to some other form of obstruction of the duct.

As a symptom chyluria is usually intermittent, being dependent upon the position of the body, character of the food, digestion, amount of fluid taken, exercise, etc. In rare cases chyluria may appear during childbirth and gradually cease after delivery, to return again during the next parturition. Such cases may be explained as due to temporary lymph stasis. Symptoms of pain in the back, groin, perineum, or testicles may accompany or precede the appearance of the chyle in the urine. When the chyluria persists over a long period of time the patient may become greatly anemic and emaciated, and finally die of exhaustion.

Serous or chylous œdema of the pelvic tissues, abdominal wall, genitalia, legs, etc., *lymph scrotum*, *lymphocele*, *chylocele*, *elephantiasis*, etc., are also conditions pointing to obstruction of the thoracic duct.

Prognosis.—This is dependent wholly upon the nature of the obstruction. It is favorable only in those cases in which the cause can be removed, or, the cause being non-malignant, the lymphatic circulation can again be restored through recanalization of a thrombus, establishment of adequate collaterals, etc. Filarial obstruction is rarely cured, but the patient may live many years in spite of it, unless the amount of chyle lost is very great and the drain persistent.

Rupture of the thoracic duct in the cervical region is given a good prognosis, as the wound may heal spontaneously or surgical treatment result successfully. Spontaneous healing of rupture of the duct in the thoracic or abdominal cavities also takes place. In some cases, in spite of surgical treatment, the patient rapidly becomes emaciated and dies from exhaustion. In general, it may be said that the prognosis in cases of thoracic duct disease with symptoms of obstruction is grave.

Treatment.—The physician's part in the treatment of disease of the thoracic duct is largely confined to symptomatic measures. His function is in the majority of cases the diagnosis of the condition and the preparation of the patient for the surgeon, in case he considers surgical interference justifiable. Beyond the first diagnostic aspiration, tapping should not be carried out except as a final necessity, since the loss of large quantities of chyle weakens the patient. Peritoneal absorption of the effusion should be permitted as much as possible. The food should be concentrated, and a diet easily digested and absorbed by the stomach should be advised. The amount of fluid taken should be restricted. In the majority of cases the ultimate treatment becomes surgical.

2. DISEASES OF THE SMALLER LYMPHATICS

General Considerations.—The lymphatic capillaries consist of a simple endothelial tube. The system is believed to be wholly a closed one, and an open communication of the lymph capillaries with the so-called "tissue spaces" is now doubted by the majority of writers. The intimate relationship of the smaller lymphatics to the tissue parenchyma is such that a clinical separation of diseases of the former from

those of the latter is well-nigh impossible. The larger lymphatic vessels have distinct walls, somewhat resembling those of the veins, but in the arrangement of the elastic tissue more like the smaller arteries. In the larger trunks an inner and outer elastic limiting membrane may be distinguished. The larger vessels possess numerous valves. Even in the case of the main lymphatic trunks only a limited number of conditions can be separated as independent affections. Of these, inflammation, obstruction, ectasia and tumors constitute the most important. Œdema, localized or general, and elephantiasis become the most important clinical manifestations resulting from lymphatic disease.

Lymphangitis.—*Simple acute lymphangitis* is a very common affection. It occurs most frequently in association with infected wounds of the hands or feet, and is usually due to streptococci, although staphylococci, gonococci, and pneumococci may be found at times. The bacteria either pass directly into the lymph vessel from the infected wound or invade the wall of the vessel from without. Wounds received during surgical operations or autopsies, infected "hang-nails," corns, cryptogenic infections of the hair follicles, etc., are among the most common forerunners of lymphangitis; but localized inflammation of the lymphatics independent of any primary focus of infection is far from uncommon. Such forms of lymphangitis are found particularly about the lips, nose, mouth, throat, penis, and vulva.

The majority of the above forms of lymphangitis are frankly surgical, and their thorough consideration is out of place in a work on internal medicine. Nevertheless, lymphangitis as a secondary phenomenon or complication plays a part of practical importance in general medicine. It occurs not infrequently during the course of the acute infectious diseases, particularly in scarlet fever, smallpox, measles, diphtheria, etc. It is frequently associated with herpes. In some individuals severe colds are preceded or accompanied by a localized lymphangitis of the lips or nostrils that may or may not go on to the development of herpetic lesions. Erysipelas is frequently complicated by a typical lymphangitis. Of the chronic specific infectious diseases, gonorrhœa, syphilis, and tuberculosis are especially likely to show an incidental lymphangitis, due, however, to the specific agent of infection rather than to a secondary pyogenic infection. Lymphangitis is a constant feature of bubonic plague. Other forms of lymphangitis are those arising after Röntgen irradiation, sunburn, contact with poison ivy or sumach, bites and stings of insects, etc.

Pathology.—Three forms of acute lymphangitis occur—*simple, purulent and proliferative*. In the simple form the wall of the lymphatic and the tissue immediately about it (perilymphangitis) are hyperemic, œdematous, infiltrated with cells, and may present small hemorrhages. The wall becomes thickened, the endothelium swells, and comes to resemble epithelium. It may become necrotic and desquamate, or it may manifest proliferative activity. Coagulation of the lymph within the vessel may occur (thrombolympfangitis), or it may remain fluid. After the cessation of the cause of the inflammation the exudate may be quickly absorbed, and with the regeneration of the damaged endothelium the normal

conditions are restored. A persistence of the exciting cause may lead to a chronic process.

In the *purulent* form there is a marked thickening of the wall of the lymphatic due to a purulent infiltration. The endothelium is swollen or desquamated, and the lumen becomes filled with pus or with a fibrino-purulent mass (purulent thrombolympangitis). The collection of pus in the lumen in the intervals between the valves gives a beaded appearance to the inflamed lymphatic. Suppuration may occur and the vessel be completely destroyed at the site of the process, so that the vessel enters into an abscess cavity. An extensive phlegmonous process may be set up in the neighboring tissues. As the result of the transportation of bacteria to the regional lymph glands, secondary abscesses are produced in the latter, and a condition of septicopyemia may result.

An acute *proliferative exudative endolympangitis* occurs in gonorrhœa, and is usually associated with a perilympangitis. The lymphatic vessel becomes greatly thickened and its lumen gradually obliterated by a fibroblastic proliferation of its walls. The endothelium may also proliferate. The gonococci can be demonstrated in the lymphatic vessel and in the tissues outside. Similar acute proliferative forms of lymphangitis may occur in the case of other infections, particularly in syphilis.

Symptoms.—The symptoms of acute *simple* lymphangitis are a localized area of redness and swelling, œdema, a painful feeling of tension, pain on movement, etc. The inflammation advances from the periphery, and as a new area becomes involved the one first affected loses its redness and swelling. When a large lymphatic trunk is involved the course of the vessel is shown by a wavy red line extending up the limb, slightly elevated above the surface, having a slightly beaded, cord-like feel, and very painful on pressure. In severe cases the line of inflammation may be an inch or so broad; in slight cases the red lines are very narrow. When the deep lymphatic vessels are alone involved the only sign present may be that of tenderness on deep pressure. The lymph glands are swollen and painful, and the portion of the limb below the seat of inflammation may become œdematous. A varying degree of fever accompanies simple lymphangitis.

In the case of *purulent* lymphangitis the local and general symptoms are much more severe. The reddened cord-like swelling is more marked and more distinctly beaded. Pressure is much more painful. Small abscesses may form along the vessel as well as in the regional lymph glands, or the entire lymphatic may suppurate. An extensive phlegmonous infiltration may then result, or a large abscess cavity may be formed. Extensive œdema of the region drained by the affected lymphatic may develop. The general condition is worse, the fever is usually high, the pain severe, and there is marked prostration. Chills and sweating may alternate in the early stages. The final picture is often that of a septicopyemia.

The chief symptoms of the *proliferative* form of lymphangitis are the thickening of the lymphatics and the development of a marked local œdema. Otherwise the clinical picture is similar to that of the other forms, although the general symptoms are usually less severe.

Diagnosis.—Lymphangitis must be distinguished from phlebitis. The general symptoms are alike, but in phlebitis the thrombosed vein when palpable is felt as a larger and deeper-seated cord, less painful on pressure. The skin is but slightly reddened or not at all, the regional lymph glands are rarely involved, while the pain is less and the fever not so high.

In the microscopic diagnosis of lymphangitis the fact that the lymphatics are filled with leukocytes is not in itself to be taken as a sign of inflammation, particularly in the case of the appendix or intestinal wall, where such collections of leukocytes in the lymphatics occur during the digestion process, or as the result of a temporary lymph stasis.

Prognosis.—The simple form usually recovers in a short time, the length of the course of the affection depending upon the general condition of the patient. Recovery is delayed in cachectic and enfeebled patients. In the purulent form the prognosis is graver, since the danger of pyemia or septicemia is great. After extensive suppuration of a lymphatic vessel or group of vessels a condition of chronic œdema of the region concerned may develop, and perfect recovery is not likely.

Treatment.—An evident cause of infection should be removed according to proper surgical methods. Extreme tension may be relieved by incision. In the involvement of the lymphatics of an extremity the limb should be elevated and complete rest enjoined. In the case of small, localized areas of lymphangitis hot or cold antiseptic dressings may be applied. Particularly in the case of the "sore nose" or "sore lip," coming so frequently under the physician's notice, do hot moist antiseptic compresses lessen the discomfort and apparently shorten the process. Early treatment may prevent the formation of herpes. In many of these cases, it should be remembered, the localized lymphangitis of the respiratory openings is often a forerunner to a severe catarrhal inflammation of the respiratory tract. Such cases should, therefore, be treated with a view of preventing the further extension or generalization of the infection. Patients who have the symptom of localized painful swellings of the lips or nose, either with or without herpes, should be put to bed and supporting and eliminating treatment carried out. The local application of astringent solutions rarely does any good.

Simple lymphangitis may be successfully treated by local and general methods without resorting to surgical measures, but all cases of purulent lymphangitis should be regarded as surgical affections. The general treatment of such cases consists also of supporting and eliminating measures. A liberal soft diet should be advised, the bowels should be kept open, and tonics and stimulants administered according to indications. Likewise, the degree of pain and prostration must govern the use of sedatives, hypnotics, or analgesics. Massage and various measures such as bandages, casts, hydro- and electrotherapy may be necessary after the process has subsided to combat the stiffness and œdema.

Chronic Lymphangitis.—Chronic inflammation of the lymphatics may be caused by the presence of parasites (*filariae*) within the lymph vessels, chronic infections (gonorrhœa, syphilis, tuberculosis, etc.), absorption of products from neighboring ulcers or abscesses, extension of malignant tumors into the lymphatics, etc. In the lymph capillaries

the endothelial cells become swollen or hypertrophic, so that in sections the vessels may resemble gland ducts or be mistaken for strands or cords of carcinoma cells. In the large lymphatics there may occur further a proliferation and induration of the connective tissue of the vessel wall and of the surrounding tissues (*perilymphangitis*). This may in time lead to a complete obliteration of the vessel. Pathologically there may, therefore, be distinguished the forms known as *endolymphangitis proliferans* or *productiva* and *lymphangitis productiva* and *fibrosa obliterans*. As the result of the obliteration of the lymph vessels a chronic œdema and elephantiasis of the region tributary to the affected vessels may develop. Productive and obliterative lymphangitis is very common in inflamed serous membranes and in the lungs. In the latter the obliteration of the lymphatics as the result of chronic inflammation plays a very important part in the production of anthracosis and in the development of later affections of the lungs, particularly in the case of pneumoconiosis. In the case of the "dust diseases" of the lungs there develops a chronic perilymphangitis involving the pleural interlobular and peribronchial lymphatics. As the result of the obliteration of the lymphatics lymph transportation to the bronchial nodes is diminished, and pulmonary infections are less easily taken care of. In the event of the occurrence of a croupous pneumonia in such a lung non-resolution or a delayed resolution is likely to result. The processes of phagocytosis are reduced. An obliterative lymphangitis is very common in the lymph vessels leading from a part affected by a malignant tumor, even when no extension of the growth into the lymphatics has occurred.

Only when the large lymph trunks or the superficial lymphatics are the seat of chronic inflammation are clinical symptoms evident. Chronic œdema, elephantiasis, lymphorrhagia, lymph fistula, chyluria, etc., are the most important clinical features. In the case of superficial lymphatics the thickened and indurated vessels may be felt as firm cord-like structures. The involvement of a local plexus of lymphatics may give rise to a tumor-like formation (lymphangioma circumscriptum, etc.).

Treatment.—This is concerned chiefly with the removal of the etiological factor and the improvement of the lymph stasis, œdema, or elephantiasis that may have resulted. The latter is partly surgical and in part medical. In the latter case the indications are similar to those for the treatment of acute lymphangitis.

Tuberculosis.—Secondary tuberculosis of the lymph vessels is very common, particularly in those of the mesentery and intestine. In the superficial vessels of the extremities it is more rare, and occurs usually in association with lupus or tuberculous ulcers of the hands or feet. Miliary tubercles may be found in the walls of the lymph vessels leading from the affected part, or the vessel may be diffusely enlarged, appearing as a firm, cord-like structure. Abscesses may develop along its course. In the leg a string of nodules or abscesses may be found along the saphenous vein. Tuberculous lymphangitis occurs also in the lymphatic vessels running to the axillary nodes in association with primary tuberculosis of the mamma. As the result of a retrograde metastasis within the superficial lymphatics of the thorax, tuberculous abscesses may develop

in cases of mammary tuberculosis at any point in the skin of the affected side of the thorax. The axillary glands are always involved. In the extension of pulmonary tuberculosis the pleural, interlobular and peribronchial lymphatics play a very important part, as the infection spreads along these channels, often giving rise to beaded rows of miliary tubercles along their course.

In the lymphatics of the mesentery and intestine a more or less marked tuberculous lymphangitis and perilymphangitis may be observed in cases of intestinal tuberculosis. The course of the lymph vessels may be shown by a tortuous string of grayish-white nodules corresponding to tubercles within or near the lymph vessels. The blocking of the vessel lumen by the tubercles or by caseous detritus may lead to a lymph stasis. Tuberculosis of the thyroid is sometimes the result of a retrograde lymphogenous extension from tuberculous cervical nodes.

Treatment.—The local treatment of tuberculous lymphangitis is chiefly surgical. The medical treatment is of tuberculosis in general.

Syphilis.—The lymph vessels in the neighborhood of the primary sore are always the seat of a more or less marked syphilitic inflammation, often showing as cord-like swellings leading from the genitalia to the inguinal nodes. In the neighborhood of secondary lesions the lymphatics are likewise involved. In the late stages a local or generalized thickening of the walls of the lymphatics may occur, and rarely gummata may be found developing within the walls of the large lymph trunks.

Other Specific Infections.—In chronic glanders (rare in man) and in leprosy specific involvement of the lymphatics may take place, giving rise to cord-like thickenings (the so-called “farcy-pipes” of the horse).

Lymphangiectasia.—Dilatation of the smaller peripheral lymphatics results from an obstruction or obliteration of the larger trunks when the collateral circulation is inadequate. Such an obliteration may be the result of a proliferative endolymphangitis, tuberculosis, carcinomatous infiltration of the wall of the lymph vessel, syphilis, etc., or an obstruction to the lymph flow may be due to the presence of parasites, pressure upon the lymph vessels, contraction of the surrounding tissue (perilymphangitis), removal or disease of the regional lymph glands, etc. In the superficial lymphatics ectasia is in the great majority of cases, if not in all, associated with or is the result of a chronic inflammation. In the mesentery dilatation of the chyle vessels is often the result of a tuberculous lymphangitis. In the dilated vessels a hypertrophy of the unstriated muscle fibers may take place.

The smaller branches of the obstructed trunks usually show the dilatation in the most marked degree. In the mesentery the dilatation of the smaller lymphatics manifests itself in the form of localized cysts (chyle cysts) or as a more extensive varicosity of a lymph plexus. When the dilatation is marked, lymphorrhagia may occur, giving rise to *chylous ascites*. A similar condition in the lymphatics of the thorax may lead to *chylothorax*. In the skin the dilatation of the lymphatics leads to a chronic oedema of the affected area, and with this there may be associated a connective-tissue hyperplasia, giving rise to the condition known clinically as *pachydermia* or *elephantiasis lymphangiectatica*.

when involving an extensive area, or, when localized, appearing as a variety of *lymphangioma*.

Œdema.—The part played by the lymphatic vessels in the production of œdema is not a simple one, and all of the factors entering into it are not clearly understood at the present time. There is normally a continuous circulation of fluid from the bloodvessels through the tissue spaces and through the cells themselves, and into the lymphatics or back again into the bloodvessels. In this circulation the fluid must pass through two sets of membranes composed of endothelial cells, the vascular and the lymphatic. The view is no longer held that any direct communication exists between the tissue spaces and the lumen of the lymphatic channels. Under normal conditions the distribution and circulation of the fluids coming from the blood into the tissues takes place in such a manner that there is at no time any excessive accumulation of fluid in the cells or tissue spaces. There is a complex physical and chemical mechanism for maintaining the fluids of the body at an approximately constant level. Under certain conditions, however, a disproportion between the inflow and outflow may occur and there results an excessive amount of fluid in the tissues (œdema) and body cavities (ascites, hydrothorax, hydropericardium, etc.). The part played by the lymphatic vessels in the production of such accumulations of fluid is a complex one partly mechanical (obstruction to the lymphatic outflow) and partly the result of vital or secretory changes in the lymphatic endothelium itself. About the latter we know but little. The results of lymphatic obstruction are better known. Venous and lymphatic outflow are apparently compensatory to each other, since we know that ligation of the veins of an extremity causes an increased outflow from the lymphatic trunk or increase of tissue fluid. Also, obstruction of the lymphatic trunk alone will not always produce œdema if the venous outflow is not hindered, as long as cardiac efficiency is maintained. A point will be reached, however, when factors favoring the production of œdema will arise, either through cardiac inefficiency, changes in filtration pressure, venous and lymphatic obstruction, changes in tissue osmotic pressure, alterations in the endothelium, etc. It is not necessary to discuss here the various theories of lymph and œdema formation. As far as the lymphatic vessels themselves are concerned, it appears from experimental investigations that the mechanical obstruction to the outflow of lymph rarely plays a primary part in the production of œdema. The abundant collateral lymphatics usually suffice to take care of the situation, even when a main trunk is obstructed; therefore, a lymph stasis is not the essential factor in producing œdema of the tissues, but it may essentially increase an œdema due to other causes. Much more important in the production of œdema are alterations in the lymphatic wall. These may affect both the amount and character of the lymph, as well as its circulation. Pathological conditions, such as lymphangitis, toxic and infective injuries to the lymphatic endothelium, etc., may lead to an increased transudation or to an hydropic swelling of the tissues. The obturation of the damaged lymphatics by lymph thrombi becomes an accessory factor in the production of an increased amount of tissue fluid.

Elephantiasis Lymphangiectatica or Lymphangitica.—Synonyms.—Pachydermia; elephantiasis Arabum; morbus herculeus; spargosis; tropical big leg; pucnemia tropica; phlegmasia Malabarica; mal de Cayenne; Barbadoes leg; sarcoma mucosum; hypersarcosis. The term elephantiasis Arabum was formerly used in a very loose way to designate a great variety of conditions in which there was a local enlargement of the tissues, particularly those of the skin. At the present time the use of the term has been narrowed to those affections of the skin and subcutaneous tissues characterized by a hyperplasia of the connective tissue, either diffuse, or localized to the bloodvessels, lymph vessels, or nerves. A lipomatous form also occurs. The most common variety is that one involving the lymphatics, its general character being a chronic and progressive enlargement of a certain portion of the body due to a hyperplasia of the connective tissue of the skin and subcutaneous tissues, hyperplasia of the lymph vessels, chronic œdema and rarely a cellular proliferation or infiltration. It occurs as an endemic disease in the tropics and sub-tropics, and as a sporadic affection throughout the remaining regions of the globe.

Etiology.—The etiology of the lymphangitic form of elephantiasis is varied. It may appear as a *spontaneous congenital* or *inherited* condition, or it may be *acquired*. The intrinsic forms involve especially the genitals and extremities. In the acquired forms of elephantiasis lymph stasis due to various etiological factors plays the most important rôle. The majority of the tropical cases are due to the presence of filaria in the lymph vessels, lymph stasis, chronic lymphangitis and chronic inflammation of the skin being produced by the presence of the parasite. The sporadic acquired cases are often the result of chronic erysipelatos or eczematous inflammations of the skin involving the lymphatic vessels. Any cause of chronic or recurring lymphangitis may lead to an elephantiasis of the affected region. Lupus, syphilis, chronic gonococcal infection, varicose ulcers (Fig. 104), frost-bite, traumatism, etc., are among the numerous etiological factors. The removal or destruction of the regional lymph glands (radical operation for carcinoma of breast, vulva, penis, etc., or destruction of inguinal nodes by chancroid) may be followed by elephantiasis of the part tributary to the glands. The condition may be temporary or permanent. Chronic œdema due to thrombophlebitis may also form the basis for the development of an elephantoid condition. Congenital acquired cases have been observed, apparently due to an intra-uterine infection. In adult males with chronic posterior urethritis and stricture an inflammatory elephantiasis of the scrotum is not rare. The *spontaneous* forms of elephantiasis are those in which the *anlage* of the condition is apparently an intrinsic one, the disease developing slowly without any exciting cause or signs of inflammation. Such cases, even when developing in adult life, are regarded as congenital or inherited. In some instances a definite family history of inheritance of the affection is present. The disease occurs at all ages, but naturally is most frequent in adults. Males are more frequently affected in the tropics; in temperate regions the majority of the sporadic cases occur in women.

Pathology.—The legs and external genitals are most frequently involved, although the affection may occur in any superficial part of the body. Next to the lower extremities and genitals, the hand, arm, face, ears, and mammae are involved, in frequency according to the order given. The affected parts may be hard and indurated (*elephantiasis dura*), or soft and pitting on pressure (*elephantiasis mollis*). The epidermis may be smooth (*elephantiasis glabra*), papillary or warty (*e. papillaris* or *verrucosa*), or nodular (*e. tuberosa*). The horny layer may be greatly thickened, presenting the appearances of ichthyosis. The

FIG. 104



Acquired elephantiasis due to varicose ulcers.

skin may be pale, shining, and more translucent than normal, or it may be more or less pigmented (*e. fusca* or *nigra*). The natural folds of skin are greatly exaggerated and the surfaces between them are usually moist and have an offensive odor. Ulcers, abscesses, chronic eczema, secondary atrophic and degenerative changes complicate the picture. The affected parts increase greatly in bulk and weight; the scrotum may attain a weight of 100 pounds or more, while the extremities may exceed in circumference the trunk. From ulcerated surfaces a large amount of lymph may escape (*lymphorrhagia*). The fluid is often milky white.

Varicose lymph vessels are sometimes seen on the surface, which may rupture and a *lymph fistula* result. This is more frequent in the lymphangiectatic form and particularly when the genitals are involved.

The microscopic examination of tissue showing the lymphangitic form of elephantiasis reveals a hyperplasia of connective tissue and lymph vessels. The new fibrous tissue may be very poor in cells, or it may resemble a cellular granulation tissue. The lymph capillaries are dilated, and there is usually marked œdema. A definite new formation of lymph vessels appears to take place and the walls of the existing lymphatics become thickened. The intermuscular connective tissue may become greatly increased and the muscles gradually destroyed. Osteomata may develop in the new-formed connective tissue, and the bones may become irregularly thickened as the result of a periostitis ossificans. Eventually, atrophy or necrosis of the bones may result. The pathological picture in all cases of lymphangitic elephantiasis is practically the same, no matter how varied the etiology.

Symptoms.—The early symptoms of elephantiasis vary greatly according to the cause. In the spontaneous forms there may be no symptoms except the resulting deformity, and in advanced cases the secondary symptoms arising from pressure, ulceration, etc. The endemic or parasitic form (filarial elephantiasis) has a definite clinical picture of infection. The sporadic cases due to erysipelatous or eczematous inflammations affecting the lymph vessels of the skin have also a definite symptomatology according to the nature of the cutaneous condition. Chills, fever, swelling of the regional lymph glands, etc., may precede or accompany the development of the condition. When due to a chronic lymph stasis unattended by inflammatory changes, the condition develops gradually out of a chronic œdema without special symptoms.

The local discomfort may be great. In all forms of elephantiasis severe neuralgic pains may attend the enlargement of the part, but in the later stages a certain degree of anesthesia results from the destruction of the nerve trunks and endings. The deformity gives great annoyance, and the effect upon the general character and disposition may be very marked. Insanity, suicide, melancholia, etc., may result from the nervous worry. The great bulk and weight of the affected part may make the patient helpless or greatly interfere with his movements. Dislocation of the affected extremity is not infrequent, and in the later stages fractures of the bone may occur. Elephantiasis of the genitals usually leads to an interference with or a loss of the sexual function. The patient's unhappy state is increased by secondary ulcers, fissures, etc.

The condition of elephantiasis develops usually very slowly, but in some cases there is a very rapid growth, large tumors being formed in a short time. This is especially true of the sporadic cases of the vulva. Ordinarily it takes years for tumors the size of a hen's egg to form, but in some cases the tumors quickly reach a great size. Such forms are often mistaken for sarcoma.

Prognosis.—In so far as the elephantoid condition itself is concerned, the prognosis is not good except in those cases in which surgical treatment is possible. The condition itself does not shorten the patient's life, with

the exception of those cases complicated by secondary infections. The chances for an improvement in the cases due to simple lymph stasis are good under appropriate treatment.

Treatment.—The sporadic cases met in temperate climates are best treated by the improvement or removal of the etiological factors. Varicose ulcers should be promptly healed; the venous outflow should be aided by position, bandages, etc. All causes of inflammation should be combated. In the case of the chronic erysipelatous or eczematous conditions of the skin, or in recurring local lymphangitis, vaccines may be prepared and used. The chronic œdema of the arm following the removal of the axillary glands may be prevented from developing into elephantiasis by the proper use of bandages, massage, warmth, etc. Such cases often recover spontaneously after a number of months. If, by proper treatment, during this time the condition is reduced to a minimum and secondary infections prevented, the elephantoid hyperplasia may be inhibited so that with the restoration of the lymphatic circulation in the axilla the extremity resumes either wholly or in part its normal condition. The ultimate treatment of advanced cases becomes surgical. Elephantiasis of the scrotum is today treated with temporary success at least by the surgical removal of the greater part of the elephantoid tissue. When the penis has been imbedded in the mass plastic repair may restore sexual potency. Ligation of the arteries has resulted in cures. Resection or stretching of the sciatic nerve, removal or amputation of the affected portions are among the surgical measures advocated. Roentgen-ray irradiation has yielded good results in some cases of congenital elephantiasis by inhibiting further growth. The general treatment in these cases is along supporting and antiseptic lines.

Neoplasms.—Tumors arising from or composed of lymph vessels are of very frequent occurrence. They may be divided into two classes, the *lymphangiomas* and the *endotheliomas*. The first-named are benign, while the second class is in part benign and in part malignant.

Lymphangioma.—The neoplasms classed as lymphangiomas consist for the chief part of spaces lined with endothelium and containing lymph. The walls of these lymph spaces may be thick or very thin; in either case the lymph spaces themselves may be small or ectatic (*lymphangioma simplex* or *cysticum*). These growths occur chiefly in the skin and subcutaneous tissue, but may be found also in internal organs. They may be diffuse or circumscribed, flat or nodular, and in the skin are frequently attended by a marked pigmentation of the epidermis and by an overgrowth of hair (nevus). In many cases it is impossible to say whether the condition represents an actual new formation of lymph vessels or simply a dilatation of preëxisting ones, with a secondary hyperplasia of the vessel walls. Lymph stasis plays a very important role in the development of some of these lymphangiomatous conditions. Those forms in which an actual proliferation and new formation of lymph vessels occurs may be classed with the true neoplasms. The most common clinical forms of the lymphangioma are certain varieties of pigmented spots and patches, nevi, warts, moles, etc., of the skin and tongue, the diffuse cavernous lymphangiomata of the tongue and lips known as

macroglossia and macrocheilia, the cystic tumors of the neck (*hygroma cysticum colli congenitum*) and the cystic lymphangiomatous tumors of the arm, trunk, mesentery and thighs. These tumors are for the greater part congenital, and may be so large at birth as to hinder delivery. They are all primarily disturbances of development, in which a true neoplasia may later develop. Melanotic sarcoma of the skin has its origin in the pigmented nevus.

Endotheliomas.—Neoplasms arising through the proliferation of endothelium either of the bloodvessels or lymphatic vessels may be classed as endotheliomas. Those arising from the endothelium of the lymphatics (*lymphangio-endothelioma* or *endothelioma lymphangiomatosum*) will alone be considered here. These belong histogenetically to the connective-tissue tumors; the benign forms may be classed with the typical varieties of this group, while the malignant forms are analogous to the sarcomata (*lymphangiosarcoma*). In general, the malignant endotheliomas are relatively less malignant than sarcomas. The very cellular endotheliomas are not necessarily malignant, since many of this nature are found in the parotid gland running clinically a perfectly benign course. On the other hand, the endotheliomas of the inner meninges are usually very malignant. Many writers deny the existence of a distinct class of endotheliomas, preferring to group these neoplasms either with the lymphangiomas, sarcomas or even the carcinomas. Undoubtedly many of the cases, if not all, reported in the literature as endotheliomas of the serous membranes have been in reality carcinoma metastases.

The most common clinical forms of the endothelioma are the fleshy wart (*lymphangioma hypertrophicum*), the endotheliomas arising from the lymph spaces of the peritoneum, pleuræ, dura mater and inner meninges, the endothelial tumors of the salivary glands, mammæ, testes, and ovaries, and more rarely those occurring in the face, mouth, uterus, etc. In the case of the endothelial tumors of the serous membranes the growth of the endothelium in the lymph capillaries gives rise to a microscopic picture suggesting the structure of an epithelial tumor, adenoma, or carcinoma; and these neoplasms are often diagnosed as the latter. Many of the tumor forms known as psammoma and cylindroma belong to the endotheliomas. The endothelial tumors of the salivary glands show a special inclination to mucoid degeneration.

Prognosis.—In the case of the great majority of the lymphangiomas of the skin the neoplasm runs a benign course, and aside from cosmetic reasons occasions no trouble. Many of them are easily removed and do not return. In other forms, as, for example, the *lymphangioma circumscriptum* of the skin, recurrence usually takes place. Malignant change sometimes occurs, as, for instance, the not infrequent development of melanotic sarcoma in pigmented lymphangiomas of the skin. In general, the endotheliomas of the salivary glands (*mixed tumors*), dura mater and skin run a relatively benign course, particularly the first named. Those of the inner meninges and serous membranes have about the same degree of malignancy as sarcomas. The endotheliomas of the mammæ, ovaries and uterus are much less malignant than sarcoma or

carcinoma of these organs, metastases being less frequent and the course longer.

Treatment.—The treatment is purely surgical. Electrolysis, Roentgen irradiation, excision, etc., are other methods advocated.

Secondary Neoplasms.—The smaller lymphatics form the chief highway by which the local spread of carcinoma takes place. The carcinoma cells break directly into the lymph capillaries, dilate them, and grow in them as solid plugs or cords of cells. The wall of the lymph vessel may become thickened, but may remain uninvolved by the cancer cells for some time. Such carcinomatous outgrowths in the lymphatics may be seen at some distance from the primary tumor, and are often regarded as metastases, whereas serial sections show their direct continuity with the primary. This is particularly true of the lymphatic vessels running from the mamma to the axillary glands; in cases of mammary cancer such vessels often appear as solid cords of tumor cells. The lymphatic capillary plexuses over an extensive area may be completely infiltrated by carcinoma in some cases, as in secondary carcinoma of the pleura or peritoneum, where the lymphatics of the entire surface may appear thickened and beaded like a rosary (*lymphangitis carcinomatosa*), and filled with carcinoma plugs. Retrograde lymphogenous metastasis of carcinoma is also very common.

Nevertheless, certain forms of sarcoma extend by preference through the lymphatics, as, for example, *lymphosarcoma*, *chondrosarcoma*, and certain sarcomas of the bones. All of the forms of sarcoma arising from *free* mesoblastic cells (chloroma, aleukemic and leukemic lymphocytoma, myeloid leukemia, etc.) extend through the lymphatics as well as through the bloodvessels. The spread of a malignant *endothelioma* is likewise largely accomplished by means of the lymph vessels.

Treatment.—This is purely surgical. The important point is the necessity of removing a large area of apparently normal tissues about the primary growth in order to get out the extensions into the neighboring lymphatics.

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